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FILE 'WPINDEX' ACCESS NOT AUTHORIZED

=> s (heat (w) shock (w) protein or charperone or HSP60 or HSP65) and vascular (s)
(disorder or disease)
L1          33 FILE ADISCTI
L2           1 FILE ADISINSIGHT
L3           0 FILE ADISNEWS
L4           0 FILE AGRICOLA
L5           0 FILE ANABSTR
L6           0 FILE AQUASCI
L7           0 FILE BIOBUSINESS
L8           0 FILE BIOCOMMERCE
L9        1137 FILE BIOSIS
L10         10 FILE BIOTECHDS
L11         28 FILE BIOTECHNO
L12          3 FILE CABA
L13         12 FILE CANCERLIT
L14         63 FILE CAPLUS
L15          0 FILE CEABA-VTB
L16          0 FILE CEN
L17          0 FILE CIN
L18          0 FILE CONFSCI
L19          0 FILE CROPB
L20          0 FILE CROPU
L21          1 FILE DISSABS
L22        334 FILE DGENE
L23          0 FILE DRUGB
L24          0 FILE DRUGMONOG2
L25          0 FILE IMSDRUGNEWS
L26         57 FILE DRUGU
L27          0 FILE IMSRESEARCH
L28          1 FILE EMBAL
L29         96 FILE EMBASE
L30         35 FILE ESBIOBASE
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'VASCULAR (S) '
L31         30 FILE FEDRIP
L32          0 FILE FOMAD
L33          0 FILE FOREGE
L34          0 FILE FROSTI
L35          0 FILE FSTA
L36          0 FILE GENBANK
L37          0 FILE HEALSAFE
L38         12 FILE IFIPAT
```

```
L39           0 FILE IMSPRODUCT
L40         268 FILE JICST-EPLUS
L41           0 FILE KOSMET
L42          11 FILE LIFESCI
L43           0 FILE MEDICONF
L44          42 FILE MEDLINE
L45           0 FILE NIOSHTIC
L46           0 FILE NTIS
L47           0 FILE NUTRACEUT
L48           0 FILE OCEAN
L49         461 FILE PASCAL
L50           0 FILE PCTGEN
L51           0 FILE PHAR
L52           0 FILE PHARMAML
L53           0 FILE PHIC
L54           2 FILE PHIN
L55           6 FILE PROMT
L56           0 FILE PROUSDDR
L57           0 FILE RDISCLOSURE
L58          77 FILE SCISEARCH
L59           0 FILE SYNTHLINE
L60          49 FILE TOXCENTER
L61         643 FILE USPATFULL
L62          45 FILE USPAT2
L63           0 FILE VETB
L64           1 FILE VETU
L65          22 FILE WPIDS
L66           0 FILE WPIFV

TOTAL FOR ALL FILES
L67        3480 (HEAT (W) SHOCK (W) PROTEIN OR CHARPERONE OR HSP60 OR HSP65)
                AND VASCULAR (S) (DISORDER OR DISEASE)

=>  s (heat (w) shock (w) protein or charperone or HSP60 or HSP65) (s) ( vascular (s)
(disorder or disease)
UNMATCHED LEFT PARENTHESIS 'S) ( VASCULAR'
The number of right parentheses in a query must be equal to the
number of left parentheses.

=> s (heat (w) shock (w) protein or charperone or HSP60 or HSP65) (s) ( vascular (s)
(disorder or disease ))
L68           0 FILE ADISCTI
L69           0 FILE ADISINSIGHT
L70           0 FILE ADISNEWS
L71           0 FILE AGRICOLA
L72           0 FILE ANABSTR
L73           0 FILE AQUASCI
L74           0 FILE BIOBUSINESS
L75           0 FILE BIOCOMMERCE
L76           9 FILE BIOSIS
L77           8 FILE BIOTECHDS
L78          17 FILE BIOTECHNO
L79           3 FILE CABA
L80          10 FILE CANCERLIT
L81          15 FILE CAPLUS
L82           0 FILE CEABA-VTB
L83           0 FILE CEN
L84           0 FILE CIN
L85           0 FILE CONFSCI
L86           0 FILE CROPB
L87           0 FILE CROPU
L88           1 FILE DISSABS
L89         326 FILE DGENE
L90           0 FILE DRUGB
L91           0 FILE DRUGMONOG2
L92           0 FILE IMSDRUGNEWS
```

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L93           2 FILE DRUGU
L94           0 FILE IMSRESEARCH
L95           1 FILE EMBAL
L96          62 FILE EMBASE
L97          34 FILE ESBIOBASE
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'VASCULAR (S) '
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'HSP65) (S) '
L98          30 FILE FEDRIP
L99           0 FILE FOMAD
L100          0 FILE FOREGE
L101          0 FILE FROSTI
L102          0 FILE FSTA
L103          0 FILE GENBANK
L104          0 FILE HEALSAFE
L105          3 FILE IFIPAT
L106          0 FILE IMSPRODUCT
L107          6 FILE JICST-EPLUS
L108          0 FILE KOSMET
L109         11 FILE LIFESCI
L110          0 FILE MEDICONF
L111          7 FILE MEDLINE
L112          0 FILE NIOSHTIC
L113          0 FILE NTIS
L114          0 FILE NUTRACEUT
L115          0 FILE OCEAN
L116         32 FILE PASCAL
L117          0 FILE PCTGEN
L118          0 FILE PHAR
L119          0 FILE PHARMAML
L120          0 FILE PHIC
L121          0 FILE PHIN
L122          0 FILE PROMT
L123          0 FILE PROUSDDR
L124          0 FILE RDISCLOSURE
L125         54 FILE SCISEARCH
L126          0 FILE SYNTHLINE
L127          6 FILE TOXCENTER
L128         76 FILE USPATFULL
L129          0 FILE USPAT2
L130          0 FILE VETB
L131          0 FILE VETU
L132          7 FILE WPIDS
L133          0 FILE WPIFV

TOTAL FOR ALL FILES
L134        720 (HEAT (W) SHOCK (W) PROTEIN OR CHARPERONE OR HSP60 OR HSP65)
                (S) (VASCULAR (S) (DISORDER OR DISEASE ))

=> s (heat (w) shock (w) protein and  HSP60 or HSP65) (s) ( vascular (s) (disorder or
disease ))
PROXIMITY OPERATION NOT ALLOWED
Certain operators may not be nested in combination with other
operators.  A nested operator is valid only when it occurs at the same
level or above the operator outside the nested phrase as determined by
the following precedence list:

                    1.    Numeric
                    2.    (W), (NOTW), (A), (NOTA)
                    3.    (S), (NOTS)
                    4.    (P), (NOTP)
                    5.    (L), (NOTL)
                    6.    AND, NOT
                    7.    OR
```

For example, '(MONOCLONAL(W)ANTIBOD?)(L)ANTIGEN?' is valid since (W) is above (L) on the precedence list. However, '((THIN(W)LAYER)(L)PHOSPHOLIPID#)(A)LACTONE#' is not valid since (L) is below (A) on the precedence list. The only exception is the 'OR' operator. This operator may be used in combination with any other operator. For example, '(ATOMIC OR NUCLEAR)(W)REACTOR' is valid.

=> s (heat (w) shock (w) protein and (HSP60 or HSP65)) (s) (vascular (s) (disorder or disease))
PROXIMITY OPERATION NOT ALLOWED
Certain operators may not be nested in combination with other operators. A nested operator is valid only when it occurs at the same level or above the operator outside the nested phrase as determined by the following precedence list:

1. Numeric
2. (W), (NOTW), (A), (NOTA)
3. (S), (NOTS)
4. (P), (NOTP)
5. (L), (NOTL)
6. AND, NOT
7. OR

For example, '(MONOCLONAL(W)ANTIBOD?)(L)ANTIGEN?' is valid since (W) is above (L) on the precedence list. However, '((THIN(W)LAYER)(L)PHOSPHOLIPID#)(A)LACTONE#' is not valid since (L) is below (A) on the precedence list. The only exception is the 'OR' operator. This operator may be used in combination with any other operator. For example, '(ATOMIC OR NUCLEAR)(W)REACTOR' is valid.

=> s heat (w) shock (w) protein and (HSP60 or HSP65) (s) (vascular (s) (disorder or disease))
L135 0 FILE ADISCTI
L136 0 FILE ADISINSIGHT
L137 0 FILE ADISNEWS
L138 0 FILE AGRICOLA
L139 0 FILE ANABSTR
L140 0 FILE AQUASCI
L141 0 FILE BIOBUSINESS
L142 0 FILE BIOCOMMERCE
L143 3 FILE BIOSIS
L144 0 FILE BIOTECHDS
L145 4 FILE BIOTECHNO
L146 0 FILE CABA
L147 2 FILE CANCERLIT
L148 4 FILE CAPLUS
L149 0 FILE CEABA-VTB
L150 0 FILE CEN
L151 0 FILE CIN
L152 0 FILE CONFSCI
L153 0 FILE CROPB
L154 0 FILE CROPU
L155 0 FILE DISSABS
L156 3 FILE DGENE
L157 0 FILE DRUGB
L158 0 FILE DRUGMONOG2
L159 0 FILE IMSDRUGNEWS
L160 0 FILE DRUGU
L161 0 FILE IMSRESEARCH
L162 1 FILE EMBAL
L163 9 FILE EMBASE
L164 6 FILE ESBIOBASE
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH FIELD CODE - 'AND' OPERATOR ASSUMED 'VASCULAR (S) '
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH FIELD CODE - 'AND' OPERATOR ASSUMED 'HSP65) (S) '

```
L165          0 FILE FEDRIP
L166          0 FILE FOMAD
L167          0 FILE FOREGE
L168          0 FILE FROSTI
L169          0 FILE FSTA
L170          0 FILE GENBANK
L171          0 FILE HEALSAFE
L172          0 FILE IFIPAT
L173          0 FILE IMSPRODUCT
L174          1 FILE JICST-EPLUS
L175          0 FILE KOSMET
L176          2 FILE LIFESCI
L177          0 FILE MEDICONF
L178          3 FILE MEDLINE
L179          0 FILE NIOSHTIC
L180          0 FILE NTIS
L181          0 FILE NUTRACEUT
L182          0 FILE OCEAN
L183          3 FILE PASCAL
L184          0 FILE PCTGEN
L185          0 FILE PHAR
L186          0 FILE PHARMAML
L187          0 FILE PHIC
L188          0 FILE PHIN
L189          0 FILE PROMT
L190          0 FILE PROUSDDR
L191          0 FILE RDISCLOSURE
L192          7 FILE SCISEARCH
L193          0 FILE SYNTHLINE
L194          3 FILE TOXCENTER
L195          4 FILE USPATFULL
L196          0 FILE USPAT2
L197          0 FILE VETB
L198          0 FILE VETU
L199          1 FILE WPIDS
L200          0 FILE WPIFV

TOTAL FOR ALL FILES
L201         56 HEAT (W) SHOCK (W) PROTEIN AND (HSP60 OR HSP65) (S) (VASCULAR
                (S) (DISORDER OR DISEASE ))

=> d l201 1-56 ibib abs

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ACCESSION NUMBER:    2000:436729  BIOSIS
DOCUMENT NUMBER:     PREV200000436729
TITLE:               Elevated levels of circulating heat shock
                     protein 70 (Hsp70) in peripheral and renal vascular
                     disease.
AUTHOR(S):           Wright, Barbara H.; Corton, Julia M.; El-Nahas, A. Meguid;
                     Wood, Richard F. M.; Pockley, A. Graham [Reprint author]
CORPORATE SOURCE:    Section of Surgery, Division of Clinical Sciences (NGH),
                     Clinical Sciences Centre, Northern General Hospital,
                     Herries Road, Sheffield, S5 7AU, UK
SOURCE:              Heart and Vessels, (2000) Vol. 15, No. 1, pp. 18-22. print.
                     CODEN: HEVEEO. ISSN: 0910-8327.
DOCUMENT TYPE:       Article
LANGUAGE:            English
ENTRY DATE:          Entered STN: 11 Oct 2000
                     Last Updated on STN: 10 Jan 2002
AB   Heat shock proteins (Hsp) are families of
     phylo-genetically conserved molecules that have a range of cytoprotective
     and intracellular functional roles.  Reactivity to heat
     shock proteins has been implicated in the development of
     autoimmune disease and tissue expression of heat shock
     proteins and increased levels of anti-Hsp antibodies have also
```

been reported in vascular disease. This study compared circulating levels of **Hsp60** and Hsp70 and antihuman **Hsp60**, antihuman Hsp70, and antimycobacterial **Hsp65** antibodies in peripheral (PVD) and renal (RVD) **vascular disease** with those in age- and sex-matched controls. Levels of Hsp70 were higher in both PVD (median 580 vs 40; $P < 0.01$) and RVD (median 160 vs 0; $P < 0.03$), whereas there were no differences in Hsp60 levels. Anti-Hsp60 antibody levels were elevated in PVD (146 vs 81 arbitrary units/ml; $P < 0.04$), but not RVD. This is the first study to demonstrate increased levels of circulating Hsp70 in pathological disease states; however, its physiological role remains to be determined.

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ACCESSION NUMBER: 1998:116507 BIOSIS
DOCUMENT NUMBER: PREV199800116507
TITLE: Effect of combined heat, ozonation and ultraviolet irradiation (VasoCare) on **heat shock protein** expression by peripheral blood leukocyte populations.
AUTHOR(S): Bulmer, J.; Bolton, A. E.; Pockley, A. G. [Reprint author]
CORPORATE SOURCE: Div. Clin. Sci., Clin. Sci. Cent., Northern General Hosp., Herries Rd., Sheffield S5 7AU, UK
SOURCE: Journal of Biological Regulators and Homeostatic Agents, (July-Sept., 1997) Vol. 11, No. 3, pp. 104-110. print.
CODEN: JBRAER. ISSN: 0393-974X.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 5 Mar 1998
Last Updated on STN: 5 Mar 1998

AB The re-administration of whole blood subjected to heat, ozonation and ultraviolet irradiation (VasoCare therapy) has been shown to elicit clinical benefits in individuals with vascular disease. Given that these stressors induce **heat shock protein** (Hsp) expression and that **heat shock protein** reactivity is implicated in the pathogenesis of **vascular disease**, this study assessed the effect of VasoCare on intracellular expression of **Hsp60** and Hsp 70 by treated peripheral blood leukocytes. Contrary to expectations, VasoCare induced a significant reduction (apprx 40%) in the proportion of peripheral blood mononuclear cells expressing intracellular Hsp60 and Hsp70, whereas it had no effect on **heat shock protein** expression by peripheral blood neutrophils. Cell surface **heat shock protein** expression was not detectable. The reduced expression of Hsp60 by mononuclear cells was concomitant with an increase in the levels of Hsp60 in treated plasma. Although the mechanism underlying the clinical effectiveness of VasoCare therapy has yet to be established, it may be that re-administration of treated blood or soluble factors derived there from modifies in vivo immune responsiveness to **heat shock proteins** or associated molecules.

L201 ANSWER 3 OF 56 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1994:207726 BIOSIS
DOCUMENT NUMBER: PREV199497220726
TITLE: Intestinal expression and cellular immune responses to human **heat-shock protein** 60 in Crohn's disease.
AUTHOR(S): Baca-Estrada, Maria E.; Gupta, Radhey S.; Stead, Ron H.; Croitoru, Kenneth [Reprint author]
CORPORATE SOURCE: Room 4H17, Intestinal Dis. Res. Program, McMaster Univ. Med. Cent., 1200 Main St. W., Hamilton, ON L8N 3Z5, Canada
SOURCE: Digestive Diseases and Sciences, (1994) Vol. 39, No. 3, pp. 498-506.
CODEN: DDSCDJ. ISSN: 0163-2116.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 10 May 1994

Last Updated on STN: 10 May 1994

AB Changes in the intestinal expression of the endogenous human 60-kDa **heat-shock protein** (HSP60) were investigated inpatients with Crohn's disease. **HSP60** immunoreactivity was detected in epithelial cells, **vascular** smooth muscle, and nerve cell bodies of both small and large bowel from patients with Crohn's **disease**. However, control tissue showed a similar pattern of HSP60 expression. Western blot analysis confirmed that the HSP60 immunoreactivity detected in the intestine corresponded to the 60-kDa HSP. The proliferative response of peripheral blood lymphocytes (PBL) and intestinal intraepithelial lymphocytes (IEL) to recombinant human HSP60 was examined. The results indicate that there was no significant difference in responses between patients with Crohn's disease and controls. Furthermore, there was no increase in the proportion of gamma/delta T cell receptor-bearing T cells in PBL from patients with Crohn's disease cultured for six days in the presence of human HSP60 as compared to control patients. These results suggest that endogenous human HSP60 is unlikely to be a target for an autoimmune response in patients with Crohn's disease.

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ACCESSION NUMBER: 2001:32328528 BIOTECHNO

TITLE: Comparative study on antibodies to human and bacterial 60 kDa **heat shock proteins** in a large cohort of patients with coronary heart disease and healthy subjects

AUTHOR: Prohaszka Z.; Duba J.; Horvath L.; Csaszar A.; Karadi I.; Szebeni A.; Singh M.; Fekete B.; Romics L.; Fust G.

CORPORATE SOURCE: Dr. Z. Prohaszka, 3rd Department of Medicine, Semmelweis University, Kutvolgyi ut 4, H-1125 Budapest, Hungary.

SOURCE: European Journal of Clinical Investigation, (2001), 31/4 (285-292), 36 reference(s)
CODEN: EJCIB8 ISSN: 0014-2972

DOCUMENT TYPE: Journal; Article

COUNTRY: United Kingdom

LANGUAGE: English

SUMMARY LANGUAGE: English

AN 2001:32328528 BIOTECHNO

AB Background: Recent observations indicate an association between antibodies against mycobacterial **heat shock protein** (**hsp65**) and coronary heart **disease** (CHD). Previously, we reported on marked differences in antigen specificity and complement activating ability of anti-**hsp65** antibodies and auto-antibodies against human **heat shock protein**, **hsp60**. Here, we investigated whether there are differences between antih-sp65 and anti-**hsp60** antibodies in their association with CHD. Design: We measured by ELISA the levels of antibodies to **hsp65**, **hsp60** and E. coli-derived GroEL in three groups: Group I, 357 patients with severe CHD who underwent by-pass surgery; Group II, 67 patients with negative coronary angiography; Group III, 321 healthy blood donors. Antibodies against Helicobacter pylori were also measured by commercial ELISA. Results: As calculated by multiple regression analysis, the levels of anti-**hsp60** autoantibodies were significantly higher in Group I compared to Group II ($P = 0.007$) or Group III ($P < 0.0001$). By contrast, although concentrations of anti-**hsp65** and anti-GroEL antibodies in Group I were higher than in Group III, no significant differences between Group I and Group II were found. Antibodies to the two bacterial hsp strongly correlated to each other, but either did not correlate or weakly correlated to **hsp60**. In Group I, serum concentrations of anti-H. pylori antibodies significantly correlated with those of anti-**hsp65** and anti-GroEL antibodies but they did not correlate with the anti-**hsp60** antibodies. Conclusion: As to their clinical relevance, a remarkable difference become evident between antibodies to

human **hsp60** and antibodies against bacterial hsp in the extent of association with CHD. On the basis of these findings and some pertinent literature data, an alternative explanation for the association between high level of anti-hsp antibodies and atherosclerotic **vascular diseases** is raised.

L201 ANSWER 5 OF 56 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN
ACCESSION NUMBER: 2000:30627004 BIOTECHNO
TITLE: Circulating **heat shock protein** 60 is associated with early cardiovascular disease
AUTHOR: Pockley A.G.; Wu R.; Lemne C.; Kiessling R.; De Faire U.; Frostegard J.
CORPORATE SOURCE: Dr. A.G. Pockley, Division of Clinical Sciences (NGH), Clinical Sciences Centre, Northern General Hospital, Herries Road, Sheffield S5 7AU, United Kingdom. E-mail: g.pockley@sheffield.ac.uk
SOURCE: Hypertension, (2000), 36/2 (303-307), 44 reference(s) CODEN: HPRTDN ISSN: 0194-911X
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 2000:30627004 BIOTECHNO
AB The phylogenetically conserved nature of **heat shock proteins** (Hsp) has led to the proposition that they may provide a link between infection and the inflammatory component to **vascular disease**. Hypertension is associated with atherosclerosis. Here, we measured circulating **heat shock protein** and **heat shock protein** antibody levels in association with borderline hypertension. Seventy-two men with borderline hypertension patients and 75 normotensive control subjects (diastolic blood pressure 85 to 94 and <80 mm Hg, respectively) were selected from a population-screening program. The levels of **Hsp60**; Hsp70; and anti-human **Hsp60**, anti-human Hsp70, and anti-mycobacterial **Hsp65** antibodies were determined with enzyme immunoassay. The presence of carotid atherosclerosis and the intima-media thickness values were determined with ultrasonography. A major novel observation in this report was the detection of circulating **Hsp60**, which was present at a significantly enhanced level in patients with borderline hypertension. Furthermore, serum **Hsp60** was associated with intima-media thicknesses ($P<0.01$). Anti-**Hsp65** antibody levels were higher in borderline hypertension ($P<0.001$), whereas Hsp70 and anti-Hsp70 antibody levels did not differ. In contrast to anti-**Hsp65** antibody, anti-**Hsp60** antibody levels were lower in borderline hypertension ($P<0.03$), although the difference was quantitatively small. None of the parameters evaluated were associated with atherosclerosis, metabolic factors, or smoking. We identified elevated **Hsp60** levels in patients with borderline hypertension and an association between early atherosclerosis and **Hsp60** levels. The physiological role of **Hsp60** release has yet to be defined, but given the proinflammatory properties, these proteins could be involved in the induction/progression of both hypertension and atherosclerosis, as well as being markers for early cardiovascular **disease**.

L201 ANSWER 6 OF 56 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN
ACCESSION NUMBER: 2000:30012965 BIOTECHNO
TITLE: Cutting edge: **Heat shock protein** (HSP) 60 activates the innate immune response: CD14 is an essential receptor for HSP60 activation of mononuclear cells
AUTHOR: Kol A.; Lichtman A.H.; Finberg R.W.; Libby P.; Kurt-Jones E.A.
CORPORATE SOURCE: Dr. E.A. Kurt-Jones, Infectious Disease Program, Dana Farber Cancer Institute, 44 Binney Street, Boston, MA

02115, United States.
SOURCE: Journal of Immunology, (01 JAN 2000), 164/1 (13-17), 43 reference(s)
CODEN: JOIMA3 ISSN: 0022-1767
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 2000:30012965 BIOTECHNO
AB **Heat shock proteins** (HSP), highly conserved across species, are generally viewed as intracellular proteins thought to serve protective functions against infection and cellular stress. Recently, we have reported the surprising finding that human and chlamydial **HSP60**, both present in human atheroma, can activate **vascular** cells and macrophages. However, the transmembrane signaling pathways by which extracellular **HSP60** may activate cells remains unclear. CD14, the monocyte receptor for LPS, binds numerous microbial products and can mediate activation of monocytes/macrophages and endothelial cells, thus promoting the innate immune response. We show here that human **HSP60** activates human PBMC and monocyte-derived macrophages through CD14 signaling and p38 mitogen-activated protein kinase, sharing this pathway with bacterial LPS. These findings provide further insight into the molecular mechanisms by which extracellular HSP may participate in atherosclerosis and other inflammatory **disorders** by activating the innate immune system.

L201 ANSWER 7 OF 56 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN
ACCESSION NUMBER: 1998:29131895 BIOTECHNO
TITLE: Clonidine-induced **heat-shock protein** expression in rat aorta
AUTHOR: Moen R.J.; LaVoi K.P.; Zhang M.; Blake M.J.
CORPORATE SOURCE: Dr. M.J. Blake, Dept. of Pharmacology and Toxicology, Univ. of North Dakota School of Med., 501 N. Columbia Road, Grand Forks, ND 58203, United States.
SOURCE: Journal of Cardiovascular Pharmacology and Therapeutics, (1998), 3/2 (171-184), 35 reference(s)
CODEN: JCPTFE ISSN: 1074-2484
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 1998:29131895 BIOTECHNO
AB Background: Restraint-stress and administration of drugs that precipitate hypertension induce **heat-shock protein** (HSP) expression in the aorta. The exact mechanism supporting this hypertension-related HSP response is unclear because HSP induction is blocked by receptor-selective and nonselective antihypertensive agents. Methods and Results: To identify mechanisms contributing to the pharmacological/physiological regulation of the HSP response in cardiovascular tissues, we administered clonidine to awake and freely moving animals to determine its effect on HSP expression in vivo. Inconsistent with previous work, we found that clonidine produced a dose-dependent and transient increase in HSP70 mRNA levels in the aorta. No other tissue examined displayed an HSP response after clonidine administration. Clonidine-induced HSP expression was not restricted to the HSP70 family; HSP89α, HSP89β, and **HSP60** were also induced. Interestingly, no heat-shock element-binding activity was observed after clonidine administration, suggesting that unusual transcriptional regulatory mechanisms mediate this response. Yohimbine and nifedipine blocked HSP70 mRNA expression, whereas isoproterenol, mecamylamine, and reserpine had no effect. Conclusions: The functional consequence of HSP expression in cardiovascular tissues may be to alter the responsiveness of cells in these tissues to subsequent drug or stress exposures, thereby implicating the HSP response as an important component of cardiovascular homeostasis. If so, treatment of mammalian organisms with drugs capable of inducting selective HSP expression in

vascular tissue may alter the progression of cardiovascular **disease** processes.

L201 ANSWER 8 OF 56 CANCERLIT on STN
ACCESSION NUMBER: 2000072722 CANCERLIT
DOCUMENT NUMBER: 20072722 PubMed ID: 10604986
TITLE: Cutting edge: **heat shock protein** (HSP) 60 activates the innate immune response: CD14 is an essential receptor for HSP60 activation of mononuclear cells.
AUTHOR: Kol A; Lichtman A H; Finberg R W; Libby P; Kurt-Jones E A
CORPORATE SOURCE: Vascular Medicine and Atherosclerosis Unit, Cardiovascular Division, Brigham and Women's Hospital, Harvard Medical School, Boston, MA 02115,USA.
CONTRACT NUMBER: P50-HL56985 (NHLBI)
PO1HL48743 (NHLBI)
RO1AI31628 (NIAID)
+
SOURCE: JOURNAL OF IMMUNOLOGY, (2000 Jan 1) 164 (1) 13-7.
Journal code: 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: MEDLINE; Abridged Index Medicus Journals; Priority Journals
OTHER SOURCE: MEDLINE 2000072722
ENTRY MONTH: 200001
ENTRY DATE: Entered STN: 20000221
Last Updated on STN: 20000221

AB **Heat shock proteins** (HSP), highly conserved across species, are generally viewed as intracellular proteins thought to serve protective functions against infection and cellular stress. Recently, we have reported the surprising finding that human and chlamydial **HSP60**, both present in human atheroma, can activate **vascular** cells and macrophages. However, the transmembrane signaling pathways by which extracellular **HSP60** may activate cells remains unclear. CD14, the monocyte receptor for LPS, binds numerous microbial products and can mediate activation of monocytes/macrophages and endothelial cells, thus promoting the innate immune response. We show here that human **HSP60** activates human PBMC and monocyte-derived macrophages through CD14 signaling and p38 mitogen-activated protein kinase, sharing this pathway with bacterial LPS. These findings provide further insight into the molecular mechanisms by which extracellular HSP may participate in atherosclerosis and other inflammatory **disorders** by activating the innate immune system.

L201 ANSWER 9 OF 56 CANCERLIT on STN
ACCESSION NUMBER: 97383530 CANCERLIT
DOCUMENT NUMBER: 97383530 PubMed ID: 9239522
TITLE: Specific regulation of HSPs in human tumor cell lines by flavonoids.
AUTHOR: Morino M; Tsuzuki T; Ishikawa Y; Shirakami T; Yoshimura M; Kiyosuke Y; Matsunaga K; Yoshikumi C; Saijo N
CORPORATE SOURCE: Kureha Chemical Industry Tokyo, Japan.
SOURCE: IN VIVO, (1997 May-Jun) 11 (3) 265-70.
Journal code: 8806809. ISSN: 0258-851X.
PUB. COUNTRY: Greece
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: MEDLINE; Priority Journals
OTHER SOURCE: MEDLINE 97383530
ENTRY MONTH: 199709
ENTRY DATE: Entered STN: 19971009
Last Updated on STN: 19971009

AB While the protective role HSPs (**Heat Shock Proteins**) has been recognized against physiological stress such as heat shock, heavy metals and glucose starvation, recent progress has

revealed another aspect of HSPs in various **diseases**. HSP27 has been shown to be involved in the acquired resistance of tumor cells hyperthermic and chemotherapeutic treatment. In human breast tumors, overexpression of HSP27 is associated with a shorter **disease** -free survival period. HSP47 is thought to be a collagen specific molecular chaperone. The involvement of HSP47 in the progression of fibrosis has been reported. Aberrant expression of HSP could cause various autoimmune **diseases**. Manipulation of HSP expression, therefore, could be a therapeutic target to reduce HSP-derived detrimental cellular effects. Flavonoids are a widely distributed group of plant substances, universally present in **vascular** plants. Although the flavonoids have been known as natural plant products as long as the alkaloids, their pharmacological effects and potential medicinal uses have been little studied by comparison. Today, the picture has changed and the biological and pharmacological activities of plant flavonoids look promising. We investigated the effect of flavonoids on the expression of HSPs in human tumor cell lines. Flavonoids inhibited the expression of HSP27, HSP47, **HSP60** and HSP72/73. The results suggested the pharmacological possibilities of flavonoids in **diseases** derived from abnormal expression of HSPs.

L201 ANSWER 10 OF 56 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:693117 CAPLUS
DOCUMENT NUMBER: 135:251960
TITLE: Suppression of vascular disorders by mucosal administration of **heat shock protein** peptides
INVENTOR(S): Weiner, Howard L.; Maron, Ruth; Libby, Peter
PATENT ASSIGNEE(S): Brigham and Women's Hospital, Inc., USA
SOURCE: PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001068124	A2	20010920	WO 2001-US8351	20010315
WO 2001068124	A3	20020314		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-189855P P 20000315

AB Methods are disclosed for treating vascular disorders in mammals. The methods involve administering one or more agents selected from a **heat shock protein**, a therapeutically effective fragment and a therapeutically effective analog of a **heat shock protein** in a form suitable for mucosal administration. In some embodiments the **heat shock protein** of the method is mycobacterial HSP65. In some embodiments the **heat shock protein** is human HSP60. In some embodiments the **heat shock protein** is chlamydial HSP60. The method is of particular value in the treatment of atherosclerosis. Also disclosed are compns. useful for treating vascular disorders in mammals. The compns. include one or more agents selected from **heat shock protein**, therapeutically effective fragments and therapeutically effective analogs of the **heat shock protein** in aerosol or oral form. In some embodiments the **heat shock**

protein of the composition is mycobacterial HSP65. In some embodiments the **heat shock protein** of the method is human HSP60. In some embodiments the **heat shock protein** is chlamydial HSP60. The compns. is of particular value in the treatment of atherosclerosis.

L201 ANSWER 11 OF 56 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:624617 CAPLUS
DOCUMENT NUMBER: 135:316767
TITLE: Chlamydia pneumoniae and chlamydial **heat shock protein** 60 stimulate proliferation of human vascular smooth muscle cells via toll-like receptor 4 and p44/p42 mitogen-activated protein kinase activation
AUTHOR(S): Sasu, Sebastian; LaVerda, David; Qureshi, Nilofer; Golenbock, Douglas T.; Beasley, Debbie
CORPORATE SOURCE: Department of Medicine, Tufts University School of Medicine, Boston, MA, USA
SOURCE: Circulation Research (2001), 89(3), 244-250
CODEN: CIRUAL; ISSN: 0009-7330
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB An early component of atherogenesis is abnormal vascular smooth muscle cell (VSMC) proliferation. The presence of Chlamydia pneumoniae in many atherosclerotic lesions raises the possibility that this organism plays a causal role in atherogenesis. In this study. C pneumoniae elementary bodies (EBs) rapidly activated p44/p42 mitogen-activated protein kinases (MAPKs) and stimulated proliferation of VSMCs in vitro. Exposure of VSMCs derived from human saphenous vein to C pneumoniae EBs (3X107 inclusion forming units/mL) enhanced bromodeoxyuridine (BrdU) incorporation 12+3-fold. UV- and heat-inactivated C pneumoniae EBs also stimulated VSMC proliferation, indicating a role of direct stimulation by chlamydial antigens. However. the mitogenic activity of C pneumoniae was heat-labile. thus excluding a role of lipopolysaccharide. Chlamydial HSP60 (25 μg/mL) replicated the effect of C pneumoniae, stimulating BrdU incorporation 7+3-fold. Exposure to C pneumoniae or chlamydial hsp60 rapidly activated p44/p42 MAPK, within 5 to 10 min of exposure. In addition PD98059 and U0126, which are two distinct inhibitors of upstream MAPK kinase 112 (MEK1/2), abolished the mitogenic effect of C pneumoniae and chlamydial hsp60. Toll-like receptors (TLRs) act as sensors for microbial antigens and can signal via the p44/p42 MAPK pathway. Human VSMCs were shown to express TLR4 mRNA and protein, and a TLR4 antagonist abolished chlamydial hsp60-induced VSMC proliferation and attenuated C pneumoniae-induced MAPK activation and VSMC proliferation. Together these results indicate that C pneumoniae and chlamydial hsp60 are potent inducers of human VSMC proliferation and that these effects are mediated, at least in part, by rapid TLR4-mediated activation of p44/p42 MAPK.
REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L201 ANSWER 12 OF 56 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:842379 CAPLUS
DOCUMENT NUMBER: 134:2328
TITLE: Human **heat shock protein** 60 in diagnosis and treatment of atherosclerosis and coronary heart disease
INVENTOR(S): Singh, Mahavir; Prohaszka, Zoltan; Fust, Gyorgy; Romics, Laszlo
PATENT ASSIGNEE(S): Semmelweis University of Medicine, Hung.
SOURCE: PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000072023	A2	20001130	WO 2000-IB688	20000522
WO 2000072023	A3	20010405		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1179182	A2	20020213	EP 2000-927636	20000522
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 2000010741	A	20020219	BR 2000-10741	20000522
JP 2003502289	T2	20030121	JP 2000-620360	20000522
NO 2001005653	A	20020117	NO 2001-5653	20011120
ZA 2001009544	A	20020620	ZA 2001-9544	20011120

PRIORITY APPLN. INFO.: GB 1999-11772 A 19990521
WO 2000-IB688 W 20000522

AB The present invention concerns novel uses for human **HSP60** (**heat shock protein** 60) in methods of treatment or diagnosis of the human body, more particularly diagnostic test methods, the manufacture of diagnostic tests, and diagnostic test kits for patients with **vascular disorders** due to atherosclerosis, having a tendency to **heat shock protein**-induced complement activation, for example to myocardial **disorders** such as coronary heart **disease**. Blood samples were applied to microtiter plates coated with recombinant hHSP60 and anti-hHSP60 antibodies were allowed to bind. Unbound material was washed away and peroxidase conjugated anti-complement C4b was added to detect complement activation. There was a pos. correlation between the level of anti-hHSP60 antibodies and coronary heart disease due to atherosclerosis. Children at risk due to family history had significantly elevated levels as well.

L201 ANSWER 13 OF 56 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:97241 CAPLUS
DOCUMENT NUMBER: 128:215017
TITLE: Effect of combined heat, ozonation and ultraviolet irradiation (VasoCare) on **heat shock protein** expression by peripheral blood leukocyte populations
AUTHOR(S): Bulmer, J.; Bolton, A. E.; Pockley, A. G.
CORPORATE SOURCE: Clinical Sciences Centre, University of Sheffield, Sheffield, UK
SOURCE: Journal of Biological Regulators and Homeostatic Agents (1997), 11(3), 104-110
CODEN: JBRAER; ISSN: 0393-974X
PUBLISHER: Wichtig Editore
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The re-administration of whole blood subjected to heat, ozonation and UV irradiation (VasoCare therapy) has been shown to elicit clin. benefits in individuals with vascular disease. Given that these stressors induce **heat shock protein** (Hsp) expression and that **heat shock protein** reactivity is implicated in the pathogenesis of **vascular disease**, this study assessed the effect of VasoCare on intracellular expression of **Hsp60** and Hsp70 by treated peripheral blood leukocytes. Contrary to expectations, VasoCare induced a significant reduction (.apprx.40%) in the proportion of peripheral blood mononuclear cells expressing intracellular Hsp60 and Hsp70, whereas it had no effect on **heat shock protein** expression by peripheral blood neutrophils. Cell surface

heat shock protein expression was not detectable. The reduced expression of Hsp60 by mononuclear cells was concomitant with an increase in the levels of Hsp60 in treated plasma. Although the mechanism underlying the clin. effectiveness of VasoCare therapy has yet to be established, it may be that re-administration of treated blood or soluble factors derived therefrom modifies in vivo immune responsiveness to **heat shock proteins** or associated mols.

REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L201 ANSWER 14 OF 56 DGENE COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: AAE11757 Protein DGENE
TITLE: Treating a vascular disorder, involves administering a composition comprising **heat shock protein**, its fragment or analog, by mucosal surface, pulmonary tract, oral or enteral route, or by inhalation -
INVENTOR: Weiner H L; Maron R; Libby P
PATENT ASSIGNEE: (BGHM)BRIGHAM & WOMENS HOSPITAL INC.
PATENT INFO: WO 2001068124 A2 20010920 49p
APPLICATION INFO: WO 2001-US8351 20010315
PRIORITY INFO: US 2000-189855P 20000315
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2001-611383 [70]
DESCRIPTION: Chlamydophila pneumoniae **heat shock protein** 60 (HSP60).
AN AAE11757 Protein DGENE
AB The patent discloses methods for treating **vascular disorders** in mammals. The method involves administering a composition comprising at least one agent selected from **heat shock protein** (HSP), its fragment or analogue, through mucosal surface, pulmonary tract, oral or enteral route or by inhalation. Compositions comprising HSP are useful for treating and suppressing a **vascular disorder**, including cell-mediated immune response, an antibody-mediated immune response, cell-mediated inflammatory **disorder**, atherosclerosis, allergic angiitis, Behcet's syndrome, granulomatosis (Churg-Strauss **disease**), Cogan's syndrome, graft-versus-host **disease** (GvHD), Henoch-Schonlein purpura, Kawasaki **disease**, leucocytoclastic vasculitis, polyarteritis nodosa (PAN), microscopic polyangiitis, polyangiitis overlap syndrome, Takayasu's arteritis, temporal arteritis, transplant rejection, Wegener's granulomatosis and thromboangiitis obliterans (Buerger's **disease**). They are useful for reducing the level of proinflammatory Th1 cytokines and also for increasing the level of antiinflammatory Th2 cytokines. The present sequence is **heat shock protein** 60 (**HSP60**) from Chlamydophila pneumoniae.

L201 ANSWER 15 OF 56 DGENE COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: AAE11756 Protein DGENE
TITLE: Treating a vascular disorder, involves administering a composition comprising **heat shock protein**, its fragment or analog, by mucosal surface, pulmonary tract, oral or enteral route, or by inhalation -
INVENTOR: Weiner H L; Maron R; Libby P
PATENT ASSIGNEE: (BGHM)BRIGHAM & WOMENS HOSPITAL INC.
PATENT INFO: WO 2001068124 A2 20010920 49p
APPLICATION INFO: WO 2001-US8351 20010315
PRIORITY INFO: US 2000-189855P 20000315
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2001-611383 [70]
DESCRIPTION: Human **heat shock protein** 60 (HSP60).
AN AAE11756 Protein DGENE

AB The patent discloses methods for treating **vascular disorders** in mammals. The method involves administering a composition comprising at least one agent selected from **heat shock protein** (HSP), its fragment or analogue, through mucosal surface, pulmonary tract, oral or enteral route or by inhalation. Compositions comprising HSP are useful for treating and suppressing a **vascular disorder**, including cell-mediated immune response, an antibody-mediated immune response, cell-mediated inflammatory **disorder**, atherosclerosis, allergic angiitis, Behcet's syndrome, granulomatosis (Churg-Strauss **disease**), Cogan's syndrome, graft-versus-host **disease** (GvHD), Henoch-Schonlein purpura, Kawasaki **disease**, leucocytoclastic vasculitis, polyarteritis nodosa (PAN), microscopic polyangiitis, polyangiitis overlap syndrome, Takayasu's arteritis, temporal arteritis, transplant rejection, Wegener's granulomatosis and thromboangiitis obliterans (Buerger's **disease**). They are useful for reducing the level of proinflammatory Th1 cytokines and also for increasing the level of antiinflammatory Th2 cytokines. The present sequence is **heat shock protein** 60 (**HSP60**) from human.

L201 ANSWER 16 OF 56 DGENE COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: AAE11755 Protein DGENE
TITLE: Treating a vascular disorder, involves administering a composition comprising **heat shock protein**, its fragment or analog, by mucosal surface, pulmonary tract, oral or enteral route, or by inhalation -
INVENTOR: Weiner H L; Maron R; Libby P
PATENT ASSIGNEE: (BGHM)BRIGHAM & WOMENS HOSPITAL INC.
PATENT INFO: WO 2001068124 A2 20010920 49p
APPLICATION INFO: WO 2001-US8351 20010315
PRIORITY INFO: US 2000-189855P 20000315
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2001-611383 [70]
DESCRIPTION: Mycobacterium tuberculosis **heat shock protein** 65 (HSP65).
AN AAE11755 Protein DGENE
AB The patent discloses methods for treating **vascular disorders** in mammals. The method involves administering a composition comprising at least one agent selected from **heat shock protein** (HSP), its fragment or analogue, through mucosal surface, pulmonary tract, oral or enteral route or by inhalation. Compositions comprising HSP are useful for treating and suppressing a **vascular disorder**, including cell-mediated immune response, an antibody-mediated immune response, cell-mediated inflammatory **disorder**, atherosclerosis, allergic angiitis, Behcet's syndrome, granulomatosis (Churg-Strauss **disease**), Cogan's syndrome, graft-versus-host **disease** (GvHD), Henoch-Schonlein purpura, Kawasaki **disease**, leucocytoclastic vasculitis, polyarteritis nodosa (PAN), microscopic polyangiitis, polyangiitis overlap syndrome, Takayasu's arteritis, temporal arteritis, transplant rejection, Wegener's granulomatosis and thromboangiitis obliterans (Buerger's **disease**). They are useful for reducing the level of proinflammatory Th1 cytokines and also for increasing the level of antiinflammatory Th2 cytokines. The present sequence is **heat shock protein** 65 (**HSP65**) from Mycobacterium tuberculosis.

L201 ANSWER 17 OF 56 EMBAL COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2004193491 EMBASE Alert (EMBAL)
TITLE: Neoangiogenesis, T-lymphocyte infiltration, and **heat shock protein**-60 are biological hallmarks of an immunomediated inflammatory process in end-stage calcified aortic valve stenosis.

AUTHOR: Mazzone A.; Epistolato M.C.; De Caterina R.; Storti S.; Vittorini S.; Sbrana S.; Gianetti J.; Bevilacqua S.; Glauber M.; Biagini A.; Tanganelli P.

CORPORATE SOURCE: Dr. A. Mazzone, Dept. of Cardiol. and Cardiac Surg., Ospedale G. Pasquinucci, 54100 Massa, Italy. mazzone@ifc.cnr.it

SOURCE: Journal of the American College of Cardiology, (5 May 2004) 43/9 (1670-1676). Refs: 30.
CODEN: JACCD ISSN: 0735-1097

PUBLISHER IDENT.: S 0735-1097(04)00351-1

PUB. COUNTRY: United States

DOCUMENT TYPE: Article

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Objectives We investigated the main biomolecular features in the evolution of aortic stenosis, focusing on advanced lesions. Background "Degenerative" aortic valve stenosis shares risk factors and inflammatory similarities with atherosclerosis. Methods We compared nonrheumatic stenotic aortic valves from 26 patients undergoing surgical valve replacement (group A) and 14 surgical control patients (group B). We performed semiquantitative histological and immunohistochemical analyses on valve leaflets to measure inflammation, sclerosis, calcium, neoangiogenesis, and intercellular adhesion molecule-1 (ICAM-1) and **vascular** cell adhesion molecule-1 (VCAM-1) expression. We assessed **heat shock protein** 60 (**hsp60**) gene expression as an index of cellular stress and C-reactive protein, erythrocyte sedimentation rate, and fibrinogen as systemic inflammatory markers. Results In group A valves, we found a prevalence of calcium nodules surrounded by activated inflammatory infiltrates, neovessels, and abundant ICAM-1, VCAM-1, and **hsp60** gene expression. Specimens from group B were negative for all of these markers, except 2 of 14 positivity for **hsp60**. The presence of active inflammatory infiltrates correlated with an abundance of thin neovessels ($p < 0.01$) and **hsp60** gene expression ($p = 0.01$), whereas neoangiogenesis correlated with inflammation ($p = 0.04$), calcium ($p = 0.01$), and **hsp60** gene expression ($p = 0.04$). Conclusions "Degenerative" aortic valve stenosis appears to be a chronic inflammatory process associated with atherosclerotic risk factors. The coexistence of neoangiogenesis, T-lymphocyte infiltration, adhesion molecules, and **hsp60** gene expression indicates an active immunomediated process in the final phases of the **disease**. .COPYRGT. 2004 by the American College of Cardiology Foundation.

L201 ANSWER 18 OF 56 EMBASE on STN

ACCESSION NUMBER: 2001150238 EMBASE

TITLE: Comparative study on antibodies to human and bacterial 60 kDa **heat shock proteins** in a large cohort of patients with coronary heart disease and healthy subjects.

AUTHOR: Prohaszka Z.; Duba J.; Horvath L.; Csaszar A.; Karadi I.; Szebeni A.; Singh M.; Fekete B.; Romics L.; Fust G.

CORPORATE SOURCE: Dr. Z. Prohaszka, 3rd Department of Medicine, Semmelweis University, Kutvolgyi ut 4, H-1125 Budapest, Hungary

SOURCE: European Journal of Clinical Investigation, (2001) 31/4 (285-292).
Refs: 36
ISSN: 0014-2972 CODEN: EJCIB8

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 006 Internal Medicine
018 Cardiovascular Diseases and Cardiovascular Surgery
026 Immunology, Serology and Transplantation

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Background: Recent observations indicate an association between antibodies

against mycobacterial **heat shock protein** (**hsp65**) and coronary heart **disease** (CHD). Previously, we reported on marked differences in antigen specificity and complement activating ability of anti-**hsp65** antibodies and auto-antibodies against human **heat shock protein**, **hsp60**. Here, we investigated whether there are differences between antih-sp65 and anti-**hsp60** antibodies in their association with CHD. Design: We measured by ELISA the levels of antibodies to **hsp65**, **hsp60** and E. coli-derived GroEL in three groups: Group I, 357 patients with severe CHD who underwent by-pass surgery; Group II, 67 patients with negative coronary angiography; Group III, 321 healthy blood donors. Antibodies against Helicobacter pylori were also measured by commercial ELISA. Results: As calculated by multiple regression analysis, the levels of anti-**hsp60** autoantibodies were significantly higher in Group I compared to Group II ($P = 0.007$) or Group III ($P < 0.0001$). By contrast, although concentrations of anti-**hsp65** and anti-GroEL antibodies in Group I were higher than in Group III, no significant differences between Group I and Group II were found. Antibodies to the two bacterial hsp strongly correlated to each other, but either did not correlate or weakly correlated to **hsp60**. In Group I, serum concentrations of anti-H. pylori antibodies significantly correlated with those of anti-**hsp65** and anti-GroEL antibodies but they did not correlate with the anti-**hsp60** antibodies. Conclusion: As to their clinical relevance, a remarkable difference become evident between antibodies to human **hsp60** and antibodies against bacterial hsp in the extent of association with CHD. On the basis of these findings and some pertinent literature data, an alternative explanation for the association between high level of anti-hsp antibodies and atherosclerotic **vascular diseases** is raised.

L201 ANSWER 19 OF 56 EMBASE
on STN

ACCESSION NUMBER: 2000315931 EMBASE

TITLE: Elevated levels of circulating **heat shock protein** 70 (Hsp70) in peripheral and renal vascular disease.

AUTHOR: Wright B.H.; Corton J.M.; El-Nahas A.M.; Wood R.F.M.; Pockley A.G.

CORPORATE SOURCE: A.G. Pockley, Section of Surgery, Division of Clinical Sciences NGH, Northern General Hospital, Herries Road, Sheffield S5 7AU, United Kingdom. g.pockley@sheffield.ac.uk

SOURCE: Heart and Vessels, (2000) 15/1 (18-22).
Refs: 29
ISSN: 0910-8327 CODEN: HEVEEO

COUNTRY: Japan

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 005 General Pathology and Pathological Anatomy
006 Internal Medicine
028 Urology and Nephrology

LANGUAGE: English

SUMMARY LANGUAGE: English

AB **Heat shock proteins** (Hsp) are families of phylogenetically conserved molecules that have a range of cytoprotective and intracellular functional roles. Reactivity to **heat shock proteins** has been implicated in the development of autoimmune **disease** and tissue expression of **heat shock proteins** and increased levels of anti-Hsp antibodies have also been reported in **vascular disease**. This study compared circulating levels of **Hsp60** and Hsp70 and antihuman **Hsp60**, antihuman Hsp70, and antimycobacterial **Hsp65** antibodies in peripheral (PVD) and renal (RVD) **vascular disease** with those in age- and sex-matched controls. Levels of Hsp70 were higher in both PVD (median 580 vs 40; $P < 0.01$) and RVD (median 160 vs 0; $P < 0.03$), whereas there were no differences in **Hsp60** levels. Anti-**Hsp60** antibody levels were elevated in PVD (146 vs 81 arbitrary units/ml; $P < 0.04$), but

not RVD. This is the first study to demonstrate increased levels of circulating Hsp70 in pathological **disease** states; however, its physiological role remains to be determined.

L201 ANSWER 20 OF 56 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2000287644 EMBASE
TITLE: Circulating **heat shock protein** 60 is associated with early cardiovascular disease.
AUTHOR: Pockley A.G.; Wu R.; Lemne C.; Kiessling R.; De Faire U.; Frostegard J.
CORPORATE SOURCE: Dr. A.G. Pockley, Division of Clinical Sciences (NGH), Clinical Sciences Centre, Northern General Hospital, Herries Road, Sheffield S5 7AU, United Kingdom. g.pockley@sheffield.ac.uk
SOURCE: Hypertension, (2000) 36/2 (303-307).
Refs: 44
ISSN: 0194-911X CODEN: HPRTDN
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The phylogenetically conserved nature of **heat shock proteins** (Hsp) has led to the proposition that they may provide a link between infection and the inflammatory component to **vascular disease**. Hypertension is associated with atherosclerosis. Here, we measured circulating **heat shock protein** and **heat shock protein** antibody levels in association with borderline hypertension. Seventy-two men with borderline hypertension patients and 75 normotensive control subjects (diastolic blood pressure 85 to 94 and <80 mm Hg, respectively) were selected from a population-screening program. The levels of **Hsp60**; Hsp70; and anti-human **Hsp60**, anti-human Hsp70, and anti-mycobacterial **Hsp65** antibodies were determined with enzyme immunoassay. The presence of carotid atherosclerosis and the intima-media thickness values were determined with ultrasonography. A major novel observation in this report was the detection of circulating **Hsp60**, which was present at a significantly enhanced level in patients with borderline hypertension. Furthermore, serum **Hsp60** was associated with intima-media thicknesses ($P<0.01$). Anti-**Hsp65** antibody levels were higher in borderline hypertension ($P<0.001$), whereas Hsp70 and anti-Hsp70 antibody levels did not differ. In contrast to anti-**Hsp65** antibody, anti-**Hsp60** antibody levels were lower in borderline hypertension ($P<0.03$), although the difference was quantitatively small. None of the parameters evaluated were associated with atherosclerosis, metabolic factors, or smoking. We identified elevated **Hsp60** levels in patients with borderline hypertension and an association between early atherosclerosis and **Hsp60** levels. The physiological role of **Hsp60** release has yet to be defined, but given the proinflammatory properties, these proteins could be involved in the induction/progression of both hypertension and atherosclerosis, as well as being markers for early cardiovascular **disease**.

L201 ANSWER 21 OF 56 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2000009162 EMBASE
TITLE: Cutting edge: **Heat shock protein** (HSP) 60 activates the innate immune response: CD14 is an essential receptor for HSP60 activation of mononuclear cells.
AUTHOR: Kol A.; Lichtman A.H.; Finberg R.W.; Libby P.; Kurt-Jones E.A.
CORPORATE SOURCE: Dr. E.A. Kurt-Jones, Infectious Disease Program, Dana Farber Cancer Institute, 44 Binney Street, Boston, MA

02115, United States
SOURCE: Journal of Immunology, (1 Jan 2000) 164/1 (13-17).
Refs: 43
ISSN: 0022-1767 CODEN: JOIMA3
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 026 Immunology, Serology and Transplantation
LANGUAGE: English
SUMMARY LANGUAGE: English
AB **Heat shock proteins** (HSP), highly conserved across species, are generally viewed as intracellular proteins thought to serve protective functions against infection and cellular stress. Recently, we have reported the surprising finding that human and chlamydial **HSP60**, both present in human atheroma, can activate **vascular** cells and macrophages. However, the transmembrane signaling pathways by which extracellular **HSP60** may activate cells remains unclear. CD14, the monocyte receptor for LPS, binds numerous microbial products and can mediate activation of monocytes/macrophages and endothelial cells, thus promoting the innate immune response. We show here that human **HSP60** activates human PBMC and monocyte-derived macrophages through CD14 signaling and p38 mitogen-activated protein kinase, sharing this pathway with bacterial LPS. These findings provide further insight into the molecular mechanisms by which extracellular HSP may participate in atherosclerosis and other inflammatory **disorders** by activating the innate immune system.

L201 ANSWER 22 OF 56 EMBASE
on STN
ACCESSION NUMBER: 1999101192 EMBASE
TITLE: Clonidine-induced **heat-shock protein** expression in rat aorta.
AUTHOR: Moen R.J.; LaVoi K.P.; Zhang M.; Blake M.J.
CORPORATE SOURCE: Dr. M.J. Blake, Dept. of Pharmacology and Toxicology, Univ. of North Dakota School of Med., 501 N. Columbia Road, Grand Forks, ND 58203, United States
SOURCE: Journal of Cardiovascular Pharmacology and Therapeutics, (1998) 3/2 (171-184).
Refs: 35
ISSN: 1074-2484 CODEN: JCPTFE
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
018 Cardiovascular Diseases and Cardiovascular Surgery
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Background: Restraint-stress and administration of drugs that precipitate hypertension induce **heat-shock protein** (HSP) expression in the aorta. The exact mechanism supporting this hypertension-related HSP response is unclear because HSP induction is blocked by receptor-selective and nonselective antihypertensive agents. Methods and Results: To identify mechanisms contributing to the pharmacological/physiological regulation of the HSP response in cardiovascular tissues, we administered clonidine to awake and freely moving animals to determine its effect on HSP expression in vivo. Inconsistent with previous work, we found that clonidine produced a dose-dependent and transient increase in HSP70 mRNA levels in the aorta. No other tissue examined displayed an HSP response after clonidine administration. Clonidine-induced HSP expression was not restricted to the HSP70 family; HSP89α, HSP89β, and **HSP60** were also induced. Interestingly, no heat-shock element-binding activity was observed after clonidine administration, suggesting that unusual transcriptional regulatory mechanisms mediate this response. Yohimbine and nifedipine blocked HSP70 mRNA expression, whereas isoproterenol, mecamylamine, and reserpine had no effect. Conclusions: The functional

consequence of HSP expression in cardiovascular tissues may be to alter the responsiveness of cells in these tissues to subsequent drug or stress exposures, thereby implicating the HSP response as an important component of cardiovascular homeostasis. If so, treatment of mammalian organisms with drugs capable of inducting selective HSP expression in **vascular** tissue may alter the progression of cardiovascular **disease** processes.

L201 ANSWER 23 OF 56 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 1998186450 EMBASE
TITLE: The role of (auto-) immunity in atherogenesis.
AUTHOR: Metzler B.; Xu Q.; Wick G.
CORPORATE SOURCE: Dr. G. Wick, Inst. for Biomedical Aging Research, Austrian Academy of Sciences, Rennweg 10, A-6020 Innsbruck, Austria. IBA@oeaw.ac.at
SOURCE: Wiener Klinische Wochenschrift, (22 May 1998) 110/10 (350-355).
Refs: 36
ISSN: 0043-5325 CODEN: WKWOAO
COUNTRY: Austria
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
018 Cardiovascular Diseases and Cardiovascular Surgery
LANGUAGE: English
SUMMARY LANGUAGE: English; German

AB Recent data from different laboratories have provided evidence that the first stages of atherosclerosis are inflammatory in nature. Research in the last decades on this multifactorial **disease** has primarily focussed on the role of lipids, with only a few anectodal findings suggesting the involvement of the immune system in atherogenesis. Within the group of antigens that may be responsible for this immunoactivation during atherogenesis, **heat shock protein** (hsp) 65/60 became a serious candidate based on the fact that immunization of normocholesterolemic rabbits with **hsp65** leads to the development of arteriosclerotic lesions in the aortic intima and these primary inflammatory lesions are aggravated by a cholesterol-rich diet, thus completely resembling human fatty streaks and atherosclerotic plaques. Furthermore, T cells in atherosclerotic lesions of rabbits have been shown to react specifically with mycobacterial **hsp65**, suggesting that cell-mediated immune responses to **hsp60** are also involved in the pathogenesis of this **disease**. In a large epidemiological study we demonstrated that serum antibodies to mycobacterial **hsp65** were significantly increased in clinically healthy subjects with sonographically demonstrable carotid atherosclerosis. These antibodies crossreact with human **hsp60**. Thus, further elucidation of the role of the immune system in atherogenesis could enhance our understanding of the mechanism of this **vascular disorder**, and may lead to new therapeutic strategies for atherosclerosis.

L201 ANSWER 24 OF 56 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 1998031574 EMBASE
TITLE: Effect of combined heat, ozonation and ultraviolet irradiation (VasoCare®) on **heat shock protein** expression by peripheral blood leukocyte populations.
AUTHOR: Bulmer J.; Bolton A.E.; Pockley A.G.
CORPORATE SOURCE: A.G. Pockley, Division of Clinical Sciences, Clinical Sciences Centre, Northern General Hospital, Herries Road, Sheffield S5 7AU, United Kingdom
SOURCE: Journal of Biological Regulators and Homeostatic Agents, (1997) 11/3 (104-110).
Refs: 49
ISSN: 0393-974X CODEN: JBRAER

COUNTRY: Italy
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
025 Hematology
027 Biophysics, Bioengineering and Medical Instrumentation
029 Clinical Biochemistry
039 Pharmacy
LANGUAGE: English
SUMMARY LANGUAGE: English

AB The re-administration of whole blood subjected to heat, ozonation and ultraviolet irradiation (VasoCare® therapy) has been shown to elicit clinical benefits in individuals with **vascular disease**. Given that these stressors induce **heat shock protein** (Hsp) expression and that **heat shock protein** reactivity is implicated in the pathogenesis of **vascular disease**, this study assessed the effect of VasoCare® on intracellular expression of **Hsp60** and Hsp70 by treated peripheral blood leukocytes. Contrary to expectations, VasoCare® induced a significant reduction (.apprx. 40%) in the proportion of peripheral blood mononuclear cells expressing intracellular **Hsp60** and Hsp70, whereas it had no effect on **heat shock protein** expression by peripheral blood neutrophils. Cell surface **heat shock protein** expression was not detectable. The reduced expression of **Hsp60** by mononuclear cells was concomitant with an increase in the levels of **Hsp60** in treated plasma. Although the mechanism underlying the clinical effectiveness of VasoCare® therapy has yet to be established, it may be that re-administration of treatment blood or soluble factors derived therefrom modifies in vivo immune responsiveness to **heat shock proteins** or associated molecules.

L201 ANSWER 25 OF 56 EMBASE
on STN
ACCESSION NUMBER: 97250556 EMBASE
DOCUMENT NUMBER: 1997250556
TITLE: Specific regulation of HSPs in human tumor cell lines by flavonoids.
AUTHOR: Morino M.; Tsuzuki T.; Ishikawa Y.; Shirakami T.; Yoshimura M.; Kiyosuke Y.-I.; Matsunaga K.; Yoshikumi C.; Saijo N.
CORPORATE SOURCE: M. Morino, Chemical Industry Co. Ltd., 3-25-1 Hyakunin-cho, Shinjuku-ku, Tokyo 169, Japan
SOURCE: In Vivo, (1997) 11/3 (265-270).
Refs: 23
ISSN: 0258-851X CODEN: IVIVE4
COUNTRY: Greece
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 016 Cancer
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB While the protective role of HSPs (**Heat Shock Proteins**) has been recognized against physiological stress such as hear shock, heavy metals and glucose starvation recent progress has revealed another aspect of HSPs in various **diseases**. HSP27 has been shown to be involved in the acquired resistance of tumor cells to hyperthermic and chemotherapeutic treatment. In human breast tumors, overexpression of HSP27 is associated with a shorter **disease**-free survival period. HSP47 is thought to be a collagen specific molecular chaperone. The involvement of HSP47 in the progression of fibrosis has been reported. Aberrant expression of HSP could cause various autoimmune **diseases**. Manipulation of HSP expression, therefore, could be a therapeutic target to reduce HSP-derived detrimental cellular effects. Flavonoids are a widely distributed group of plant substances, universally present in **vascular** plants. Although the flavonoids have been known as natural plant products as long as the alkaloids, their

pharmacological effects and potential medicinal uses have been little studied by comparison. Today, the picture has changed and the biological and pharmacological activities of plant flavonoids look promising. We investigated the effect of flavonoids on the expression of HSPs in human tumor cell lines. Flavonoids inhibited the expression of HSP27, HSP47, **HSP60** and HSP72/73. The results suggested the pharmacological possibilities of flavonoids in **diseases** derived from abnormal expression of HSPs.

L201 ANSWER 26 OF 56 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 94119570 EMBASE
DOCUMENT NUMBER: 1994119570
TITLE: Intestinal expression and cellular immune responses to human **heat-shock protein** 60 in Crohn's disease.
AUTHOR: Baca-Estrada M.E.; Gupta R.S.; Stead R.H.; Croitoru K.
CORPORATE SOURCE: Intestinal Disease Research Program, McMaster University Medical Center, 1200 Main St. W.,Hamilton, Ont. L8N 3Z5, Canada
SOURCE: Digestive Diseases and Sciences, (1994) 39/3 (498-506). ISSN: 0163-2116 CODEN: DDSCDJ
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 048 Gastroenterology
006 Internal Medicine
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Changes in the intestinal expression of the endogenous human 60-kDa **heat- shock protein** (**HSP60**) were investigated in patients with Crohn's **disease**. **HSP60** immunoreactivity was detected in epithelial cells, **vascular** smooth muscle, and nerve cell bodies of both small and large bowel from patients with Crohn's **disease**. However, control tissue showed a similar pattern of **HSP60** expression. Western blot analysis confirmed that the **HSP60** immunoreactivity detected in the intestine corresponded to the 60-kDa HSP. The proliferative response of peripheral blood lymphocytes (PBL) and intestinal intraepithelial lymphocytes (IEL) to recombinant human **HSP60** was examined. The results indicate that there was no significant difference in responses between patients with Crohn's **disease** and controls. Furthermore, there was no increase in the proportion of γ/δ T cell receptor-bearing T cells in PBL from patients with Crohn's **disease** cultured for six days in the presence of human **HSP60** as compared to control patients. These results suggest that endogenous human **HSP60** is unlikely to be a target for an autoimmune response in patients with Crohn's **disease**.

L201 ANSWER 27 OF 56 Elsevier BIOBASE COPYRIGHT 2004 Elsevier Science B.V. on STN

ACCESSION NUMBER: 2004118652 ESBIOBASE
TITLE: Neoangiogenesis, T-lymphocyte infiltration, and **heat shock protein**-60 are biological hallmarks of an immunomediated inflammatory process in end-stage calcified aortic valve stenosis
AUTHOR: Mazzone A.; Epistolato M.C.; De Caterina R.; Storti S.; Vittorini S.; Sbrana S.; Gianetti J.; Bevilacqua S.; Glauber M.; Biagini A.; Tanganelli P.
CORPORATE SOURCE: Dr. A. Mazzone, Dept. of Cardiol. and Cardiac Surg., Ospedale G. Pasquinucci, 54100 Massa, Italy. E-mail: mazzone@ifc.cnr.it
SOURCE: Journal of the American College of Cardiology, (05 MAY 2004), 43/9 (1670-1676), 30 reference(s) CODEN: JACCDI ISSN: 0735-1097
PUBLISHER ITEM IDENT.: S0735109704003511
DOCUMENT TYPE: Journal; Article

COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Objectives We investigated the main biomolecular features in the evolution of aortic stenosis, focusing on advanced lesions. Background "Degenerative" aortic valve stenosis shares risk factors and inflammatory similarities with atherosclerosis. Methods We compared nonrheumatic stenotic aortic valves from 26 patients undergoing surgical valve replacement (group A) and 14 surgical control patients (group B). We performed semiquantitative histological and immunohistochemical analyses on valve leaflets to measure inflammation, sclerosis, calcium, neoangiogenesis, and intercellular adhesion molecule-1 (ICAM-1) and **vascular** cell adhesion molecule-1 (VCAM-1) expression. We assessed **heat shock protein** 60 (**hsp60**) gene expression as an index of cellular stress and C-reactive protein, erythrocyte sedimentation rate, and fibrinogen as systemic inflammatory markers. Results In group A valves, we found a prevalence of calcium nodules surrounded by activated inflammatory infiltrates, neovessels, and abundant ICAM-1, VCAM-1, and **hsp60** gene expression. Specimens from group B were negative for all of these markers, except 2 of 14 positivity for **hsp60**. The presence of active inflammatory infiltrates correlated with an abundance of thin neovessels ($p < 0.01$) and **hsp60** gene expression ($p = 0.01$), whereas neoangiogenesis correlated with inflammation ($p = 0.04$), calcium ($p = 0.01$), and **hsp60** gene expression ($p = 0.04$). Conclusions "Degenerative" aortic valve stenosis appears to be a chronic inflammatory process associated with atherosclerotic risk factors. The coexistence of neoangiogenesis, T-lymphocyte infiltration, adhesion molecules, and **hsp60** gene expression indicates an active immunomediated process in the final phases of the **disease**. .COPYRGT. 2004 by the American College of Cardiology Foundation.

L201 ANSWER 28 OF 56 Elsevier BIOBASE COPYRIGHT 2004 Elsevier Science B.V. on STN

ACCESSION NUMBER: 2001096331 ESBIOBASE
TITLE: Comparative study on antibodies to human and bacterial 60 kDa **heat shock proteins** in a large cohort of patients with coronary heart disease and healthy subjects
AUTHOR: Prohaszka Z.; Duba J.; Horvath L.; Csaszar A.; Karadi I.; Szebeni A.; Singh M.; Fekete B.; Romics L.; Fust G.
CORPORATE SOURCE: Dr. Z. Prohaszka, 3rd Department of Medicine, Semmelweis University, Kutvolgyi ut 4, H-1125 Budapest, Hungary.
SOURCE: European Journal of Clinical Investigation, (2001), 31/4 (285-292), 36 reference(s)
CODEN: EJCIB8 ISSN: 0014-2972
DOCUMENT TYPE: Journal; Article
COUNTRY: United Kingdom
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Background: Recent observations indicate an association between antibodies against mycobacterial **heat shock protein** (**hsp65**) and coronary heart **disease** (CHD). Previously, we reported on marked differences in antigen specificity and complement activating ability of anti-**hsp65** antibodies and auto-antibodies against human **heat shock protein, hsp60**. Here, we investigated whether there are differences between antih-sp65 and anti-**hsp60** antibodies in their association with CHD. Design: We measured by ELISA the levels of antibodies to **hsp65**, **hsp60** and E. coli-derived GroEL in three groups: Group I, 357 patients with severe CHD who underwent by-pass surgery; Group II, 67 patients with negative coronary angiography; Group III, 321 healthy blood donors. Antibodies against Helicobacter pylori were also measured by commercial ELISA. Results: As

calculated by multiple regression analysis, the levels of anti-**hsp60** autoantibodies were significantly higher in Group I compared to Group II (P = 0.007) or Group III (P < 0.0001). By contrast, although concentrations of anti-**hsp65** and anti-GroEL antibodies in Group I were higher than in Group III, no significant differences between Group I and Group II were found. Antibodies to the two bacterial hsp strongly correlated to each other, but either did not correlate or weakly correlated to **hsp60**. In Group I, serum concentrations of anti-H. pylori antibodies significantly correlated with those of anti-**hsp65** and anti-GroEL antibodies but they did not correlate with the anti-**hsp60** antibodies. Conclusion: As to their clinical relevance, a remarkable difference become evident between antibodies to human **hsp60** and antibodies against bacterial hsp in the extent of association with CHD. On the basis of these findings and some pertinent literature data, an alternative explanation for the association between high level of anti-hsp antibodies and atherosclerotic **vascular diseases** is raised.

L201 ANSWER 29 OF 56 Elsevier BIOBASE COPYRIGHT 2004 Elsevier Science B.V. on STN

ACCESSION NUMBER: 2000186134 ESBIOBASE
TITLE: Circulating **heat shock protein** 60 is associated with early cardiovascular disease
AUTHOR: Pockley A.G.; Wu R.; Lemne C.; Kiessling R.; De Faire U.; Frostegard J.
CORPORATE SOURCE: Dr. A.G. Pockley, Division of Clinical Sciences (NGH), Clinical Sciences Centre, Northern General Hospital, Herries Road, Sheffield S5 7AU, United Kingdom. E-mail: g.pockley@sheffield.ac.uk
SOURCE: Hypertension, (2000), 36/2 (303-307), 44 reference(s) CODEN: HPRTDN ISSN: 0194-911X
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English

AB The phylogenetically conserved nature of **heat shock proteins** (Hsp) has led to the proposition that they may provide a link between infection and the inflammatory component to **vascular disease**. Hypertension is associated with atherosclerosis. Here, we measured circulating **heat shock protein** and **heat shock protein** antibody levels in association with borderline hypertension. Seventy-two men with borderline hypertension patients and 75 normotensive control subjects (diastolic blood pressure 85 to 94 and <80 mm Hg, respectively) were selected from a population-screening program. The levels of **Hsp60**; Hsp70; and anti-human **Hsp60**, anti-human Hsp70, and anti-mycobacterial **Hsp65** antibodies were determined with enzyme immunoassay. The presence of carotid atherosclerosis and the intima-media thickness values were determined with ultrasonography. A major novel observation in this report was the detection of circulating **Hsp60**, which was present at a significantly enhanced level in patients with borderline hypertension. Furthermore, serum **Hsp60** was associated with intima-media thicknesses (P<0.01). Anti-**Hsp65** antibody levels were higher in borderline hypertension (P<0.001), whereas Hsp70 and anti-Hsp70 antibody levels did not differ. In contrast to anti-**Hsp65** antibody, anti-**Hsp60** antibody levels were lower in borderline hypertension (P<0.03), although the difference was quantitatively small. None of the parameters evaluated were associated with atherosclerosis, metabolic factors, or smoking. We identified elevated **Hsp60** levels in patients with borderline hypertension and an association between early atherosclerosis and **Hsp60** levels. The physiological role of **Hsp60** release has yet to be defined, but given the proinflammatory properties, these proteins could be involved in the induction/progression of both hypertension and atherosclerosis, as well as being markers for early cardiovascular

disease.

L201 ANSWER 30 OF 56 Elsevier BIOBASE COPYRIGHT 2004 Elsevier Science B.V. on STN
ACCESSION NUMBER: 2000005931 ESBIOBASE
TITLE: Cutting edge: **Heat shock protein** (HSP) 60 activates the innate immune response: CD14 is an essential receptor for HSP60 activation of mononuclear cells
AUTHOR: Kol A.; Lichtman A.H.; Finberg R.W.; Libby P.; Kurt-Jones E.A.
CORPORATE SOURCE: Dr. E.A. Kurt-Jones, Infectious Disease Program, Dana Farber Cancer Institute, 44 Binney Street, Boston, MA 02115, United States.
SOURCE: Journal of Immunology, (01 JAN 2000), 164/1 (13-17), 43 reference(s)
CODEN: JOIMA3 ISSN: 0022-1767
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
AB **Heat shock proteins** (HSP), highly conserved across species, are generally viewed as intracellular proteins thought to serve protective functions against infection and cellular stress. Recently, we have reported the surprising finding that human and chlamydial **HSP60**, both present in human atheroma, can activate **vascular** cells and macrophages. However, the transmembrane signaling pathways by which extracellular **HSP60** may activate cells remains unclear. CD14, the monocyte receptor for LPS, binds numerous microbial products and can mediate activation of monocytes/macrophages and endothelial cells, thus promoting the innate immune response. We show here that human **HSP60** activates human PBMC and monocyte-derived macrophages through CD14 signaling and p38 mitogen-activated protein kinase, sharing this pathway with bacterial LPS. These findings provide further insight into the molecular mechanisms by which extracellular HSP may participate in atherosclerosis and other inflammatory **disorders** by activating the innate immune system.

L201 ANSWER 31 OF 56 Elsevier BIOBASE COPYRIGHT 2004 Elsevier Science B.V. on STN
ACCESSION NUMBER: 1997182724 ESBIOBASE
TITLE: Specific regulation of HSPs in human tumor cell lines by flavonoids
AUTHOR: Morino M.; Tsuzuki T.; Ishikawa Y.; Shirakami T.; Yoshimura M.; Kiyosuke Y.-I.; Matsunaga K.; Yoshikumi C.; Saijo N.
CORPORATE SOURCE: M. Morino, Chemical Industry Co. Ltd., 3-25-1 Hyakunin-cho, Shinjuku-ku, Tokyo 169, Japan.
SOURCE: In Vivo, (1997), 11/3 (265-270), 23 reference(s)
CODEN: IVIVE4 ISSN: 0258-851X
DOCUMENT TYPE: Journal; Article
COUNTRY: Greece
LANGUAGE: English
SUMMARY LANGUAGE: English
AB While the protective role of HSPs (**Heat Shock Proteins**) has been recognized against physiological stress such as hear shock, heavy metals and glucose starvation recent progress has revealed another aspect of HSPs in various **diseases**. HSP27 has been shown to be involved in the acquired resistance of tumor cells to hyperthermic and chemotherapeutic treatment. In human breast tumors, overexpression of HSP27 is associated with a shorter **disease** -free survival period. HSP47 is thought to be a collagen specific molecular chaperone. The involvement of HSP47 in the progression of fibrosis has been reported. Aberrant expression of HSP could cause various autoimmune **diseases**. Manipulation of HSP expression, therefore, could be a therapeutic target to reduce HSP-derived

detrimental cellular effects. Flavonoids are a widely distributed group of plant substances, universally present in **vascular** plants. Although the flavonoids have been known as natural plant products as long as the alkaloids, their pharmacological effects and potential medicinal uses have been little studied by comparison. Today, the picture has changed and the biological and pharmacological activities of plant flavonoids look promising. We investigated the effect of flavonoids on the expression of HSPs in human tumor cell lines. Flavonoids inhibited the expression of HSP27, HSP47, **HSP60** and HSP72/73. The results suggested the pharmacological possibilities of flavonoids in **diseases** derived from abnormal expression of HSPs.

L201 ANSWER 32 OF 56 Elsevier BIOBASE COPYRIGHT 2004 Elsevier Science B.V. on STN

ACCESSION NUMBER: 1994079784 ESBIOBASE
TITLE: Intestinal expression and cellular immune responses to human **heat-shock protein** 60 in Crohn's disease
AUTHOR: Baca-Estrada M.E.; Gupta R.S.; Stead R.H.; Croitoru K.
CORPORATE SOURCE: K. Croitoru, Intestinal Disease Research Program, McMaster University Medical Center, 1200 Main St. W., Hamilton, Ont. L8N 3Z5, Canada.
SOURCE: Digestive Diseases and Sciences, (1994), 39/3 (498-506)
CODEN: DDSCDJ ISSN: 0163-2116
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Changes in the intestinal expression of the endogenous human 60-kDa **heat- shock protein** (**HSP60**) were investigated in patients with Crohn's **disease**. **HSP60** immunoreactivity was detected in epithelial cells, **vascular** smooth muscle, and nerve cell bodies of both small and large bowel from patients with Crohn's **disease**. However, control tissue showed a similar pattern of **HSP60** expression. Western blot analysis confirmed that the **HSP60** immunoreactivity detected in the intestine corresponded to the 60-kDa HSP. The proliferative response of peripheral blood lymphocytes (PBL) and intestinal intraepithelial lymphocytes (IEL) to recombinant human **HSP60** was examined. The results indicate that there was no significant difference in responses between patients with Crohn's **disease** and controls. Furthermore, there was no increase in the proportion of γ/δ T cell receptor-bearing T cells in PBL from patients with Crohn's **disease** cultured for six days in the presence of human **HSP60** as compared to control patients. These results suggest that endogenous human **HSP60** is unlikely to be a target for an autoimmune response in patients with Crohn's **disease**.

L201 ANSWER 33 OF 56 JICST-EPlus COPYRIGHT 2004 JST on STN

ACCESSION NUMBER: 960081665 JICST-EPlus
TITLE: Kawasaki disease and stress protein.
AUTHOR: YOKOTA SHUNPEI
CORPORATE SOURCE: Yokohama City Univ., Sch. of Med.
SOURCE: Ensho (Japanese Journal of Inflammation), (1995) vol. 15, no. 6, pp. 445-450. Journal Code: Y0899A (Fig. 3, Ref. 19)
CODEN: ENSHEE; ISSN: 0389-4290
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Commentary
LANGUAGE: Japanese
STATUS: New

AB Kawasaki **disease**, an acute febrile illness which affects infants and young children, is characterized by diffuse mucosal inflammation, indurative edema, polymorphous rash, and nonsuppurative cervical lymphadenopathy. About 15-20% of patients suffer coronary arterial damage, and they may develop myocardial infarction, chronic coronary

insufficiency, and sudden death. Since Kawasaki originally described this **disease** entity in 1967, the number of such patients in Japan has reached 100,000. While the etiology is still unknown, the epidemiological features of this **disease** indicate that it is related to an infectious agent. Immunologically, both a highly increased level of several cytokines and the activation of immunocompetent cells have been demonstrated. Pathology have revealed that the **vascular** lesion begins with endothelial cell damage, the initial step of which may be activation of the endothelial cell to express ICAM-1 and ELAM-1 by cytokines. Thus, the etiologic factor(s) would predispose to an activation of both the immune system and the endothelial cells. Some mitogenic materials including superantigen, stress protein, and so forth, would be the candidates. According to the clinical findings, inflammatory changes at the site of a previous BCG inoculation seems to be an early and specific manifestation of Kawasaki diseasse. We postulated that molecule(s) that are cross-reactive between the suspected infectious agent and the mycobacterial BCG antigen may contribute to this inflammatory process. Using BCG lysates or recombinant stress protein, **HSP65**, as antigen for Western blotting, convalescent, but not acute, phase sera of Kawasaki **disease** did react with **HSP65** antigen, suggesting bacterial stress protein may be the causative agent which abnormally activate immune system. (author abst.)

L201 ANSWER 34 OF 56 LIFESCI COPYRIGHT 2004 CSA on STN
ACCESSION NUMBER: 2000:27185 LIFESCI
TITLE: **Heat Shock Protein** (HSP) 60 Activates the Innate Immune Response: CD14 Is an Essential Receptor for HSP60 Activation of Mononuclear Cells
AUTHOR: Kol, A.; Lichtman, A.H.; Finberg, R.W.; Libby, P.; Kurt-Jones, E.A.*
CORPORATE SOURCE: Infectious Disease Program D1440, Dana Farber Cancer Institute, 44 Binney Street, Boston, MA 02115, USA; E-mail: Evelyn_Kurt-Jones@dfci.harvard.edu
SOURCE: Journal of Immunology [J. Immunol.], (20000101) vol. 164, no. 1, pp. 13-17.
ISSN: 0022-1767.
DOCUMENT TYPE: Journal
FILE SEGMENT: F
LANGUAGE: English
SUMMARY LANGUAGE: English
AB **Heat shock proteins** (HSP), highly conserved across species, are generally viewed as intracellular proteins thought to serve protective functions against infection and cellular stress. Recently, we have reported the surprising finding that human and chlamydial **HSP60**, both present in human atheroma, can activate **vascular** cells and macrophages. However, the trans-membrane signaling pathways by which extracellular **HSP60** may activate cells remains unclear. CD14, the monocyte receptor for LPS, binds numerous microbial products and can mediate activation of monocytes/macrophages and endothelial cells, thus promoting the innate immune response. We show here that human **HSP60** activates human PBMC and monocyte-derived macrophages through CD14 signaling and p38 mitogen-activated protein kinase, sharing this pathway with bacterial LPS. These findings provide further insight into the molecular mechanisms by which extracellular HSP may participate in atherosclerosis and other inflammatory **disorders** by activating the innate immune system.

L201 ANSWER 35 OF 56 LIFESCI COPYRIGHT 2004 CSA on STN
ACCESSION NUMBER: 97:8534 LIFESCI
TITLE: Insulin-dependent diabetes mellitus
AUTHOR: Tisch, R.; McDevitt, H.
CORPORATE SOURCE: Dep. Microbiol. and Immun., Sch. Med., Univ. North Carolina, Chapel Hill, NC 27599, USA
SOURCE: CELL, (1996) vol. 85, no. 3, pp. 291-297.
ISSN: 0092-8674.
DOCUMENT TYPE: Journal

TREATMENT CODE: General Review
FILE SEGMENT: F
LANGUAGE: English

AB Insulin-dependent diabetes mellitus (IDDM) is a multifactorial autoimmune **disease** for which susceptibility is determined by environmental and genetic factors. Inheritance is polygenic, with the genotype of the major histocompatibility complex (MHC) being the strongest genetic determinant. However, even in monozygotic twins, the concordance rate is only 50%, indicating the importance of a number of as yet unidentified environmental factors. There is a north-south gradient in incidence of the **disease** with the highest incidence (1%-1.5% in Finland) being in northern Europe, with decreasing incidence in more southerly and tropical locations. Although this suggests the effect of infectious agents, in the nonobese diabetic (NOD) mouse, germ-free NOD mice have the highest incidence (nearly 100%) that has been seen in any NOD colony. While MHC class II genotype is one of the strongest factors determining susceptibility to IDDM, it has long been apparent that susceptibility at MHC class II is a necessary but not sufficient predisposing genetic factor. Microsatellite analyses of genome-wide polymorphisms in multiplex IDDM families and in NOD crosses with nonsusceptible strains have identified many other genetic regions that also influence susceptibility. Thus, in the NOD mouse there are at least 15 other regions on 11 other chromosomes that contribute to genetic predisposition. In man, linkage studies have suggested an even larger number (as many as 19) genetic regions determining IDDM susceptibility. For the most part, the genes determining susceptibility in each of these chromosomal regions have yet to be identified. Several of these regions also influence susceptibility to a murine counterpart of systemic lupus erythematosus and to a murine model of multiple sclerosis. IDDM in animal models is T cell mediated and requires the participation of both CD8 super(+), class I MHC restricted and CD4 super(+), class II MHC restricted T cells. Extensive studies in rodent models have failed to identify the origins of the autoreactivity in IDDM, but demonstrate the importance of a number (8-10) of islet beta cell-expressed proteins that are the targets of the autoimmune process in this **disease**. Other studies have shown the important roles of several regulatory and proinflammatory cytokines, including interferon-gamma (IFN gamma), tumor necrosis factor alpha (TNF alpha), interleukin-4 (IL-4), and IL-10, as well as the importance of a number of accessory molecules (B7.1, B7.2) and adhesion molecules (very late antigen 4). Studies of rodent models and preliminary studies in man have shown that the completion of beta cell destruction can be considerably delayed or prevented by parenteral administration of beta cell autoantigens-including insulin, glutamic acid decarboxylase (GAD), and **heat shock protein** 60 (**HSP60**). A number of studies have also shown that manipulation of cytokine networks by administration of specific cytokines or their antagonists can delay or prevent diabetes. Together, these advances have set the stage for developing a complete molecular understanding of the pathogenesis of this autoimmune **disease** and for the design of rational and effective means of prevention. Prevention could then replace insulin therapy, which is effective but associated with long term renal, **vascular**, and retinal complications.

L201 ANSWER 36 OF 56 MEDLINE on STN
ACCESSION NUMBER: 2000448466 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11001481
TITLE: Elevated levels of circulating **heat shock protein** 70 (Hsp70) in peripheral and renal vascular disease.
AUTHOR: Wright B H; Corton J M; El-Nahas A M; Wood R F; Pockley A G
CORPORATE SOURCE: Division of Clinical Sciences, Clinical Sciences Centre, Northern General Hospital, Sheffield, UK.
SOURCE: Heart and vessels, (2000) 15 (1) 18-22.
Journal code: 8511258. ISSN: 0910-8327.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200101
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010117

AB **Heat shock proteins** (Hsp) are families of phylogenetically conserved molecules that have a range of cytoprotective and intracellular functional roles. Reactivity to **heat shock proteins** has been implicated in the development of autoimmune disease and tissue expression of **heat shock proteins** and increased levels of anti-Hsp antibodies have also been reported in vascular disease. This study compared circulating levels of **Hsp60** and Hsp70 and antihuman **Hsp60**, antihuman Hsp70, and antimycobacterial **Hsp65** antibodies in peripheral (PVD) and renal (RVD) **vascular disease** with those in age- and sex-matched controls. Levels of Hsp70 were higher in both PVD (median 580 vs 40; $P < 0.01$) and RVD (median 160 vs 0; $P < 0.03$), whereas there were no differences in Hsp60 levels. Anti-Hsp60 antibody levels were elevated in PVD (146 vs 81 arbitrary units/ml; $P < 0.04$), but not RVD. This is the first study to demonstrate increased levels of circulating Hsp70 in pathological disease states; however, its physiological role remains to be determined.

L201 ANSWER 37 OF 56 MEDLINE on STN
ACCESSION NUMBER: 1998159594 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9498159
TITLE: Effect of combined heat, ozonation and ultraviolet irradiation (VasoCare) on **heat shock protein** expression by peripheral blood leukocyte populations.
AUTHOR: Bulmer J; Bolton A E; Pockley A G
CORPORATE SOURCE: Clinical Sciences Centre, University of Sheffield, UK.
SOURCE: Journal of biological regulators and homeostatic agents, (1997 Jul-Sep) 11 (3) 104-10.
Journal code: 8809253. ISSN: 0393-974X.
PUB. COUNTRY: Italy
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199804
ENTRY DATE: Entered STN: 19980422
Last Updated on STN: 19980422
Entered Medline: 19980414

AB The re-administration of whole blood subjected to heat, ozonation and ultraviolet irradiation (VasoCare therapy) has been shown to elicit clinical benefits in individuals with vascular disease. Given that these stressors induce **heat shock protein** (Hsp) expression and that **heat shock protein** reactivity is implicated in the pathogenesis of **vascular disease**, this study assessed the effect of VasoCare on intracellular expression of **Hsp60** and Hsp70 by treated peripheral blood leukocytes. Contrary to expectations, VasoCare induced a significant reduction (approximately 40%) in the proportion of peripheral blood mononuclear cells expressing intracellular Hsp60 and Hsp70, whereas it had no effect on **heat shock protein** expression by peripheral blood neutrophils. Cell surface **heat shock protein** expression was not detectable. The reduced expression of Hsp60 by mononuclear cells was concomitant with an increase in the levels of Hsp60 in treated plasma. Although the mechanism underlying the clinical effectiveness of VasoCare therapy has yet to be established, it may be that re-administration of treated blood or soluble factors derived therefrom modifies in vivo immune responsiveness to **heat shock proteins** or associated molecules.

L201 ANSWER 38 OF 56 MEDLINE on STN

ACCESSION NUMBER: 94178159 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7907543
TITLE: Intestinal expression and cellular immune responses to human **heat-shock protein** 60 in Crohn's disease.
AUTHOR: Baca-Estrada M E; Gupta R S; Stead R H; Croitoru K
CORPORATE SOURCE: Department of Medicine, McMaster University, Hamilton, Ontario, Canada.
SOURCE: Digestive diseases and sciences, (1994 Mar) 39 (3) 498-506. Journal code: 7902782. ISSN: 0163-2116.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199404
ENTRY DATE: Entered STN: 19940428
Last Updated on STN: 19950206
Entered Medline: 19940420

AB Changes in the intestinal expression of the endogenous human 60-kDa **heat-shock protein** (HSP60) were investigated in patients with Crohn's disease. **HSP60** immunoreactivity was detected in epithelial cells, **vascular** smooth muscle, and nerve cell bodies of both small and large bowel from patients with Crohn's **disease**. However, control tissue showed a similar pattern of HSP60 expression. Western blot analysis confirmed that the HSP60 immunoreactivity detected in the intestine corresponded to the 60-kDa HSP. The proliferative response of peripheral blood lymphocytes (PBL) and intestinal intraepithelial lymphocytes (IEL) to recombinant human HSP60 was examined. The results indicate that there was no significant difference in responses between patients with Crohn's disease and controls. Furthermore, there was no increase in the proportion of gamma/delta T cell receptor-bearing T cells in PBL from patients with Crohn's disease cultured for six days in the presence of human HSP60 as compared to control patients. These results suggest that endogenous human HSP60 is unlikely to be a target for an autoimmune response in patients with Crohn's disease.

L201 ANSWER 39 OF 56 PASCAL COPYRIGHT 2004 INIST-CNRS. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2001-0215502 PASCAL
COPYRIGHT NOTICE: Copyright .COPYRGT. 2001 INIST-CNRS. All rights reserved.
TITLE (IN ENGLISH): Comparative study on antibodies to human and bacterial 60 kDa **heat shock proteins** in a large cohort of patients with coronary heart disease and healthy subjects
AUTHOR: PROHASZKA Z.; DUBA J.; HORVATH L.; CSASZAR A.; KARADI I.; SZEBENI A.; SINGH M.; FEKETE B.; ROMICS L.; FUEST G.
CORPORATE SOURCE: Semmelweis University, Budapest, Hungary; Hungarian Academy of Sciences, Budapest, Hungary; National Institute of Cardiology, Budapest, Hungary; German Center for Biotechnology and Lionex Gmbh, Braunschweig, Germany, Federal Republic of
SOURCE: European journal of clinical investigation, (2001), 31(4), 285-292, 36 refs. ISSN: 0014-2972
DOCUMENT TYPE: Journal
BIBLIOGRAPHIC LEVEL: Analytic
COUNTRY: United Kingdom
LANGUAGE: English
AVAILABILITY: INIST-5808, 354000095052730020
AN 2001-0215502 PASCAL
CP Copyright .COPYRGT. 2001 INIST-CNRS. All rights reserved.
AB Background Recent observations indicate an association between antibodies against mycobacterial **heat shock protein** (

hsp65) and coronary heart **disease** (CHD). Previously, we reported on marked differences in antigen specificity and complement activating ability of anti-**hsp65** antibodies and auto-antibodies against human **heat shock protein**, **hsp60**. Here, we investigated whether there are differences between antih-sp65 and anti-**hsp60** antibodies in their association with CHD. Design We measured by ELISA the levels of antibodies to **hsp65**, **hsp60** and E. coli-derived GroEL in three groups: Group I, 357 patients with severe CHD who underwent by-pass surgery; Group II, 67 patients with negative coronary angiography; Group III, 321 healthy blood donors. Antibodies against Helicobacter pylori were also measured by commercial ELISA. Results As calculated by multiple regression analysis, the levels of anti-**hsp60** auto-antibodies were significantly higher in Group I compared to Group II (P= 0.007) or Group III (P < 0.0001). By contrast, although concentrations of anti-**hsp65** and anti-GroEL antibodies in Group I were higher than in Group III, no significant differences between Group I and Group II were found. Antibodies to the two bacterial hsp strongly correlated to each other, but either did not correlate or weakly correlated to **hsp60**. In Group I, serum concentrations of anti-H.pylori antibodies significantly correlated with those of anti-**hsp65** and anti-GroEL antibodies but they did not correlate with the anti-**hsp60** antibodies. Conclusion As to their clinical relevance, a remarkable difference become evident between antibodies to human **hsp60** and antibodies against bacterial hsp in the extent of association with CHD. On the basis of these findings and some pertinent literature data, an alternative explanation for the association between high level of anti-hsp antibodies and atherosclerotic **vascular diseases** is raised.

L201 ANSWER 40 OF 56 PASCAL COPYRIGHT 2004 INIST-CNRS. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2000-0456178 PASCAL
COPYRIGHT NOTICE: Copyright .COPYRGT. 2000 INIST-CNRS. All rights reserved.
TITLE (IN ENGLISH): Circulating **heat shock protein** 60 is associated with early cardiovascular disease
AUTHOR: POCKLEY A. G.; RUHIA WU; LEMNE C.; KIESSLING R.; DE FAIRE U.; FROSTEGARD J.
CORPORATE SOURCE: Division of Clinical Sciences (NGH), Northern General Hospital, Herries Road, Sheffield, United Kingdom; Department of Medicine, Karolinska Hospital, Sweden; Unit of Rheumatology and CMM and of Cardiovascular Medicine, Karolinska Hospital, Sweden; Department of Medicine, Department of Epidemiology, Institute of Environmental Medicine, Karolinska Institute, Stockholm, Sweden
SOURCE: Hypertension : (Dallas, Tex. 1979), (2000), 36(2), 303-307, 44 refs.
ISSN: 0194-911X CODEN: HPRTDN
DOCUMENT TYPE: Journal
BIBLIOGRAPHIC LEVEL: Analytic
COUNTRY: United States
LANGUAGE: English
AVAILABILITY: INIST-18059, 354000091018750250

AN 2000-0456178 PASCAL
CP Copyright .COPYRGT. 2000 INIST-CNRS. All rights reserved.
AB The phylogenetically conserved nature of **heat shock proteins** (Hsp) has led to the proposition that they may provide a link between infection and the inflammatory component to **vascular disease**. Hypertension is associated with atherosclerosis. Here, we measured circulating **heat shock protein** and **heat shock protein** antibody levels in association with borderline hypertension. Seventy-two men with borderline hypertension patients and 75 normotensive control subjects (diastolic

blood pressure 85 to 94 and <80 mm Hg, respectively) were selected from a population-screening program. The levels of **Hsp60**; Hsp70; and anti-human **Hsp60**, anti-human Hsp70, and anti-mycobacterial **Hsp65** antibodies were determined with enzyme immunoassay. The presence of carotid atherosclerosis and the intima-media thickness values were determined with ultrasonography. A major novel observation in this report was the detection of circulating **Hsp60**, which was present at a significantly enhanced level in patients with borderline hypertension. Furthermore, serum **Hsp60** was associated with intima-media thicknesses ($P<0.01$). Anti-**Hsp65** antibody levels were higher in borderline hypertension ($P<0.001$), whereas Hsp70 and anti-Hsp70 antibody levels did not differ. In contrast to anti-**Hsp65** antibody, anti-**Hsp60** antibody levels were lower in borderline hypertension ($P<0.03$), although the difference was quantitatively small. None of the parameters evaluated were associated with atherosclerosis, metabolic factors, or smoking. We identified elevated **Hsp60** levels in patients with borderline hypertension and an association between early atherosclerosis and **Hsp60** levels. The physiological role of **Hsp60** release has yet to be defined, but given the proinflammatory properties, these proteins could be involved in the induction/progression of both hypertension and atherosclerosis, as well as being markers for early cardiovascular **disease**.

L201 ANSWER 41 OF 56 PASCAL COPYRIGHT 2004 INIST-CNRS. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 1994-0442035 PASCAL
COPYRIGHT NOTICE: Copyright .COPYRGT. 1994 INIST-CNRS. All rights reserved.
TITLE (IN ENGLISH): Intestinal expression and cellular immune responses to human **heat-shock protein** 60 in Crohn's disease
AUTHOR: BACA-ESTRADA M. E.; GUPTA R. S.; STEAD R. H.; CROITORU K.
CORPORATE SOURCE: McMaster univ., dep. medicien, intestinal diseases res. program, Hamilton ON L8N 3Z5, Canada
SOURCE: Digestive diseases and sciences, (1994), 39(3), 498-506, 48 refs.
ISSN: 0163-2116 CODEN: DDSCDJ
DOCUMENT TYPE: Journal
BIBLIOGRAPHIC LEVEL: Analytic
COUNTRY: United States
LANGUAGE: English
AVAILABILITY: INIST-5060, 354000049537910080
AN 1994-0442035 PASCAL
CP Copyright .COPYRGT. 1994 INIST-CNRS. All rights reserved.
AB Changes in the intestinal expression of the endogenous human 60-kDa **heat-shock protein** (**HSP60**) were investigated in patients with Crohn's **disease**. **HSP60** immunoreactivity was detected in epithelial cells, **vascular** smooth muscle, and nerve cell bodies of both small and large bowel from patients with Crohn's **disease**. However, control tissue showed a similar pattern of **HSP60** expression. Western blot analysis confirmed that the HPS60 immunoreactivity detected in the intestine corresponded to the 60-kDa HSP. The proliferative response of peripheral blood lymphocytes (PBL) and intestinal intraepithelial lymphocytes (IEL) to recombinant human HPS60 was examined

L201 ANSWER 42 OF 56 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN

ACCESSION NUMBER: 2001:375347 SCISEARCH
THE GENUINE ARTICLE: 427WT
TITLE: Comparative study on antibodies to human and bacterial 60 kDa **heat shock proteins** in a large cohort of patients with coronary heart disease and healthy subjects
AUTHOR: Prohaszka Z (Reprint); Duba J; Horvath L; Csaszar A;

Karadi I; Szebeni A; Singh M; Fekete B; Romics L; Fust G

CORPORATE SOURCE: Semmelweis Univ Med, Fac Med, Dept Med, Kutvolgyi Ut 4, H-1125 Budapest, Hungary (Reprint); Semmelweis Univ Med, Fac Med, Dept Med, H-1125 Budapest, Hungary; Hungarian Acad Sci, Res Grp Metab Genet & Immunol, Budapest, Hungary; Natl Inst Cardiol, Budapest, Hungary; Semmelweis Univ Med, Fac Hlth Sci, Dept Med & Gerontol 1, H-1125 Budapest, Hungary; German Ctr Biotechnol, Braunschweig, Germany; Lionex Gmbh, Braunschweig, Germany

COUNTRY OF AUTHOR: Hungary; Germany

SOURCE: EUROPEAN JOURNAL OF CLINICAL INVESTIGATION, (APR 2001) Vol. 31, No. 4, pp. 285-292.
Publisher: BLACKWELL SCIENCE LTD, P O BOX 88, OSNEY MEAD, OXFORD OX2 0NE, OXON, ENGLAND.
ISSN: 0014-2972.

DOCUMENT TYPE: Article; Journal

LANGUAGE: English

REFERENCE COUNT: 36

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Background Recent observations indicate an association between antibodies against mycobacterial **heat shock protein** (hsp65) and coronary heart disease (CHD). Previously, we reported on marked differences in antigen specificity and complement activating ability of anti-hsp65 antibodies and auto-antibodies against human **heat shock protein**, hsp60. Here, we investigated whether there are differences between antih-sp65 and anti-hsp60 antibodies in their association with CHD.

Design We measured by ELISA the levels of antibodies to hsp65, hsp60 and E. coli-derived GroEL in three groups: Group I, 357 patients with severe CHD who underwent by-pass surgery; Group II, 67 patients with negative coronary angiography; Group III, 321 healthy blood donors. Antibodies against Helicobacter pylori were also measured by commercial ELISA.

Results As calculated by multiple regression analysis, the levels of anti-hsp60 autoantibodies were significantly higher in Group I compared to Group II ($P = 0.007$) or Group III ($P < 0.0001$). By contrast, although concentrations of anti-hsp65 and anti-GroEL antibodies in Group I were higher than in Group III, no significant differences between Group I and Group II were found. Antibodies to the two bacterial hsp strongly correlated to each other, but either did not correlate or weakly correlated to hsp60. In Group I, serum concentrations of anti-H.pylori antibodies significantly correlated with those of anti-hsp65 and anti-GroEL antibodies but they did not correlate with the anti-hsp50 antibodies.

Conclusion As to their clinical relevance, a remarkable difference become evident between antibodies to human **hsp60** and antibodies against bacterial hsp in the extent of association with CHD. On the basis of these findings and some pertinent literature data, an alternative explanation for the association between high level of anti-hsp antibodies and atherosclerotic **vascular diseases** is raised.

L201 ANSWER 43 OF 56 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN

ACCESSION NUMBER: 2000:668510 SCISEARCH

THE GENUINE ARTICLE: 347YZ

TITLE: Elevated levels of circulating **heat shock protein** 70 (Hsp70) in peripheral and renal vascular disease

AUTHOR: Wright B H; Corton J M; ElNahas A M; Wood R F M; Pockley A G (Reprint)

CORPORATE SOURCE: NO GEN HOSP, CTR CLIN SCI, DIV CLIN SCI, SECT SURG, HERRIES RD, SHEFFIELD S5 7AU, S YORKSHIRE, ENGLAND (Reprint); NO GEN HOSP, CTR CLIN SCI, DIV CLIN SCI, SECT SURG, SHEFFIELD S5 7AU, S YORKSHIRE, ENGLAND

COUNTRY OF AUTHOR: ENGLAND

SOURCE: HEART AND VESSELS, (JAN-FEB 2000) Vol. 15, No. 1, pp. 18-22.

Publisher: SPRINGER-VERLAG, 175 FIFTH AVE, NEW YORK, NY 10010.
ISSN: 0910-8327.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: CLIN
LANGUAGE: English
REFERENCE COUNT: 29

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB **Heat shock proteins** (Hsp) are families of phylogenetically conserved molecules that have a range of cytoprotective and intracellular functional roles. Reactivity to **heat shock proteins** has been implicated in the development of autoimmune **disease** and tissue expression of **heat shock proteins** and increased levels of anti-Hsp antibodies have also been reported in **vascular disease**. This study compared circulating levels of **Hsp60** and Hsp70 and antihuman **Hsp60**, antihuman Hsp70, and antimycobacterial **Hsp65** antibodies in peripheral (PVD) and renal (RVD) **vascular disease** with those in age- and sex-matched controls. Levels of Hsp70 were higher in both PVD (median 580 vs 40; $P < 0.01$) and RVD (median 160 vs 0; $P < 0.03$), whereas there were no differences in **Hsp60** levels. Anti-**Hsp60** antibody levels were elevated in PVD (146 vs 81 arbitrary units/ml: $P < 0.04$), but not RVD. This is the first study to demonstrate increased levels of circulating Hsp70 in pathological **disease** states; however, its physiological role remains to be determined.

L201 ANSWER 44 OF 56 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 2000:654562 SCISEARCH
THE GENUINE ARTICLE: 346GP
TITLE: Circulating **heat shock protein** 60 is associated with early cardiovascular disease
AUTHOR: Pockley A G (Reprint); Wu R; Lemne C; Kiessling R; deFaire U; Frostegard J
CORPORATE SOURCE: NO GEN HOSP, CTR CLIN SCI, DIV CLIN SCI, HERRIES RD, SHEFFIELD S5 7AU, S YORKSHIRE, ENGLAND (Reprint); KAROLINSKA HOSP, DEPT MED, UNIT RHEUMATOL & CMM, S-17176 STOCKHOLM, SWEDEN; KAROLINSKA HOSP, DEPT MED, UNIT CARDIOVASC MED, S-17176 STOCKHOLM, SWEDEN; KAROLINSKA INST, INST ENVIRONM MED, DEPT MED, S-10401 STOCKHOLM, SWEDEN; KAROLINSKA INST, INST ENVIRONM MED, DEPT EPIDEMIOL, S-10401 STOCKHOLM, SWEDEN
COUNTRY OF AUTHOR: ENGLAND; SWEDEN
SOURCE: HYPERTENSION, (AUG 2000) Vol. 36, No. 2, pp. 303-307. Publisher: LIPPINCOTT WILLIAMS & WILKINS, 530 WALNUT ST, PHILADELPHIA, PA 19106-3621.
ISSN: 0194-911X.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE; CLIN
LANGUAGE: English
REFERENCE COUNT: 44

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The phylogenetically conserved nature of **heat shock proteins** (Hsp) has led to the proposition that they may provide a link between infection and the inflammatory component to **vascular disease**. Hypertension is associated with atherosclerosis. Here, we measured circulating **heat shock protein** and **heat shock protein** antibody levels in association with borderline hypertension. Seventy-two men with borderline hypertension patients and 75 normotensive control subjects (diastolic blood pressure 85 to 94 and <80 mm Hg, respectively) were selected from a population-screening program. The levels of **Hsp60**; Hsp70; and anti-human **Hsp60**, anti-human Hsp70, and anti-mycobacterial **Hsp65** antibodies were determined with enzyme immunoassay. The presence of carotid atherosclerosis and the intima-media thickness values were determined with ultrasonography. A major novel observation in this

report was the detection of circulating **Hsp60**, which was present at a significantly enhanced level in patients with borderline hypertension. Furthermore, serum **Hsp60** was associated with intima-media thicknesses (P<0.01). Anti-**Hsp65** antibody levels were higher in borderline hypertension (P<0.001), whereas Hsp70 and anti-Hsp70 antibody levels did not differ. In contrast to anti-**Hsp65** antibody, anti-**Hsp60** antibody levels were lower in borderline hypertension (P<0.03), although the difference was quantitatively small. None of the parameters evaluated were associated with atherosclerosis, metabolic factors, or smoking. We identified elevated **Hsp60** levels in patients with borderline hypertension and an association between early atherosclerosis and **Hsp60** levels. The physiological role of **Hsp60** release has yet to be defined, but given the proinflammatory properties, these proteins could be involved in the induction/progression of both hypertension and atherosclerosis, as well as being markers for early cardiovascular **disease**.

L201 ANSWER 45 OF 56 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 2000:5095 SCISEARCH
THE GENUINE ARTICLE: 266VP
TITLE: Cutting edge: **Heat shock protein** (HSP) 60 activates the innate immune response: CD14 is an essential receptor for HSP60 activation of mononuclear cells
AUTHOR: Kol A; Lichtman A H; Finberg R W; Libby P; KurtJones E A (Reprint)
CORPORATE SOURCE: HARVARD UNIV, PROGRAM INFECT DIS D1440, SCH MED, DEPT ADULT ONCOL, DANA FARBER CANC INST, BOSTON, MA 02115 (Reprint); HARVARD UNIV, PROGRAM INFECT DIS D1440, SCH MED, DEPT ADULT ONCOL, DANA FARBER CANC INST, BOSTON, MA 02115; HARVARD UNIV, BRIGHAM & WOMENS HOSP, SCH MED, CARDIOVASC DIV, VASC MED & ATHEROSCLEROSIS UNIT, BOSTON, MA 02115; HARVARD UNIV, BRIGHAM & WOMENS HOSP, SCH MED, DEPT PATHOL, DIV VASC RES, BOSTON, MA 02115
COUNTRY OF AUTHOR: USA
SOURCE: JOURNAL OF IMMUNOLOGY, (1 JAN 2000) Vol. 164, No. 1, pp. 13-17.
Publisher: AMER ASSOC IMMUNOLOGISTS, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814.
ISSN: 0022-1767.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 43
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB **Heat shock proteins** (HSP), highly conserved across species, are generally viewed as intracellular proteins thought to serve protective functions against infection and cellular stress. Recently, we have reported the surprising finding that human and chlamydial **HSP60**, both present in human atheroma, can activate **vascular** cells and macrophages, However, the transmembrane signaling pathways by which extracellular **HSP60** may activate cells remains unclear. CD14, the monocyte receptor for LPS, binds numerous microbial products and can mediate activation of monocytes/macrophages and endothelial cells, thus promoting the innate immune response. We show here that human **HSP60** activates human PBMC and monocyte derived macrophages through CD14 signaling and p38 mitogen-activated protein kinase, sharing this pathway with bacterial LPS, These findings provide further insight into the molecular mechanisms by which extracellular HSP may participate in atherosclerosis and other inflammatory **disorders** by activating the innate immune system.

L201 ANSWER 46 OF 56 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 1998:95689 SCISEARCH
THE GENUINE ARTICLE: YT541

TITLE: Effect of combined heat, ozonation and ultraviolet irradiation (VasoCare(TM)) on **heat shock protein** expression by peripheral blood leukocyte populations

AUTHOR: Bulmer J; Bolton A E; Pockley A G (Reprint)
CORPORATE SOURCE: NO GEN HOSP, CTR CLIN SCI, NGHT, DIV CLIN SCI, HERRIES RD, SHEFFIELD S5 7AU, S YORKSHIRE, ENGLAND (Reprint); UNIV SHEFFIELD, CTR CLIN SCI, SHEFFIELD S10 2TN, S YORKSHIRE, ENGLAND
COUNTRY OF AUTHOR: ENGLAND

SOURCE: JOURNAL OF BIOLOGICAL REGULATORS AND HOMEOSTATIC AGENTS, (JUL-SEP 1997) Vol. 11, No. 3, pp. 104-110.
Publisher: WICHTIG EDITORE, 72/74 VIA FRIULI, 20135 MILAN, ITALY.
ISSN: 0393-974X.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 49

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The re-administration of whole blood subjected to heat, ozonation and ultraviolet irradiation (VasoCare(TM) therapy) has been shown to elicit clinical benefits in individuals with **vascular disease**. . Given that these stressors induce **heat shock protein** (Hsp) expression and that **heat shock protein** reactivity is implicated in the pathogenesis of **vascular disease**, this study assessed the effect of VasoCare(TM) on intracellular expression of **Hsp60** and Hsp70 by treated peripheral blood leukocytes. Contrary to expectations, VasoCare(TM) induced a significant reduction (similar to 40%) in the proportion of peripheral blood mononuclear cells expressing intracellular **Hsp60** and Hsp70, whereas it had no effect on **heat shock protein** expression by peripheral blood neurophils. Cell surface **heat shock protein** expression was not detectable. The reduced expression of **Hsp60** by mononuclear cells was concomitant with an increase in the levels of **Hsp60** in treated plasma. Although the mechanism underlying the clinical effectiveness of VasoCare(TM) therapy has yet to be established it may be that re-administration of treated blood or soluble factors derived therefrom modifies in vivo immune responsiveness to **heat shock proteins** or associated molecules.

L201 ANSWER 47 OF 56 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 97:537352 SCISEARCH
THE GENUINE ARTICLE: XK377
TITLE: Specific regulation of HSPs in human tumor cell lines by flavonoids

AUTHOR: Morino M (Reprint); Tsuzuki T; Ishikawa Y; Shirakami T; Yoshimura M; Kiyosuke Y I; Matsunaga K; Yoshikumi C; Saijo N
CORPORATE SOURCE: KUREHA CHEM IND CO LTD, SHINJUKU KU, 3-25-1 HYAKUNIN CHO, TOKYO 169, JAPAN (Reprint); NATL CANC CTR, RES INST, DIV PHARMACOL, TOKYO 104, JAPAN
COUNTRY OF AUTHOR: JAPAN

SOURCE: IN VIVO, (MAY-JUN 1997) Vol. 11, No. 3, pp. 265-270.
Publisher: INT INST ANTICANCER RESEARCH, EDITORIAL OFFICE 1ST KM KAPANDNTIOU-KALAMOU RD KAPANDRITI, POB 22, ATHENS 19014, GREECE.
ISSN: 0258-851X.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 23

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB While the protective role of HSPs (**Heat Shock Proteins**) has been recognized against physiological stress such as heat shock, heavy metals and glucose starvation, recent progress has

revealed another aspect of HSPs in various **diseases**. HSP27 has been shown to be involved in the acquired resistance of tumor cells to hyperthermic and chemotherapeutic treatment. In human breast tumors, overexpression of HSP27 is associated with a shorter **disease** -free survival period. HSP47 is thought to be a collagen specific molecular chaperone. The involvement of HSP47 in the progression of fibrosis has been reported Aberrant expression of HSP could cause various autoimmune **diseases**. Manipulation of HSP expression, therefore, could be a therapeutic target to reduce HSP-derived detrimental cellular effects Flavonoids are a winery distributed group of plant substances, universally present in **vascular** plants. Although the flavanoids have been known as natural plant products as long as the alkaloids, their pharmacological effects and potential medicinal uses have been little studied by comparison. Today, the picture has changed and the biological and pharmacological activities of plant flavonoids look promising. We investigated the effect of flavonoids on the expression of HSPs in human tumor; cell lines Flavonoids inhibited the expression of HSP27, HSP47, **HSP60** and HSP72/73. The results suggested the pharmacological possibilities of flavonoids in **diseases** derived from abnormal expression of HSPs.

L201 ANSWER 48 OF 56 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 94:192556 SCISEARCH
THE GENUINE ARTICLE: NC618
TITLE: INTESTINAL EXPRESSION AND CELLULAR IMMUNE-RESPONSES TO HUMAN **HEAT-SHOCK PROTEIN**-60 IN CROHNS-DISEASE
AUTHOR: BACAESTRADA M E; GUPTA R S; STEAD R H; CROITORU K (Reprint)
CORPORATE SOURCE: MCMASTER UNIV, MED CTR, DEPT MED, INTESTINAL DIS RES PROGRAM, 1200 MAIN ST W, ROOM 4H17, HAMILTON L8N 3Z5, ONTARIO, CANADA (Reprint); MCMASTER UNIV, MED CTR, DEPT MED, INTESTINAL DIS RES PROGRAM, 1200 MAIN ST W, ROOM 4H17, HAMILTON L8N 3Z5, ONTARIO, CANADA; MCMASTER UNIV, DEPT BIOCHEM, HAMILTON L8N 3Z5, ONTARIO, CANADA; MCMASTER UNIV, DEPT PATHOL, HAMILTON L8N 3Z5, ONTARIO, CANADA
COUNTRY OF AUTHOR: CANADA
SOURCE: DIGESTIVE DISEASES AND SCIENCES, (MAR 1994) Vol. 39, No. 3, pp. 498-506.
ISSN: 0163-2116.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE; CLIN
LANGUAGE: ENGLISH
REFERENCE COUNT: 48

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Changes in the intestinal expression of the endogenous human 60-kDa **heat-shock protein** (**HSP60**) were investigated in patients with Crohn's **disease**. **HSP60** immunoreactivity was detected in epithelial cells, **vascular** smooth muscle, and nerve cell bodies of both small and large bowel from patients with Crohn's **disease**. However, control tissue showed a similar pattern of **HSP60** expression. Western blot analysis confirmed that the **HSP60** immunoreactivity detected in the intestine corresponded to the 60-kDa HSP. The proliferative response of peripheral blood lymphocytes (PBL) and intestinal intraepithelial lymphocytes (IEL) to recombinant human **HSP60** was examined. The results indicate that there was no significant difference in responses between patients with Crohn's **disease** and controls. Furthermore, there was no increase in the proportion of gamma/delta T cell receptor-bearing T cells in PBL from patients with Crohn's **disease** cultured for six days in the presence of human **HSP60** as compared to control patients. These results suggest that endogenous human **HSP60** is unlikely to be a target for an autoimmune response in patients with Crohn's **disease**.

L201 ANSWER 49 OF 56 TOXCENTER COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:66915 TOXCENTER
COPYRIGHT: Copyright 2004 ACS
DOCUMENT NUMBER: CA13518251960P
TITLE: Suppression of vascular disorders by mucosal administration of **heat shock protein** peptides
AUTHOR(S): Weiner, Howard L.; Maron, Ruth; Libby, Peter
CORPORATE SOURCE: ASSIGNEE: Brigham and Women's Hospital, Inc.
PATENT INFORMATION: WO 2001068124 A2 20 Sep 2001
SOURCE: (2001) PCT Int. Appl., 49 pp.
CODEN: PIXXD2.
COUNTRY: UNITED STATES
DOCUMENT TYPE: Patent
FILE SEGMENT: CAPLUS
OTHER SOURCE: CAPLUS 2001:693117
LANGUAGE: English
ENTRY DATE: Entered STN: 20020319
Last Updated on STN: 20020319

AB Methods are disclosed for treating vascular disorders in mammals. The methods involve administering one or more agents selected from a **heat shock protein**, a therapeutically effective fragment and a therapeutically effective analog of a **heat shock protein** in a form suitable for mucosal administration. In some embodiments the **heat shock protein** of the method is mycobacterial HSP65. In some embodiments the **heat shock protein** is human HSP60. In some embodiments the **heat shock protein** is chlamydial HSP60. The method is of particular value in the treatment of atherosclerosis. Also disclosed are compns. useful for treating vascular disorders in mammals. The compns. include one or more agents selected from **heat shock protein**, therapeutically effective fragments and therapeutically effective analogs of the **heat shock protein** in aerosol or oral form. In some embodiments the **heat shock protein** of the composition is mycobacterial HSP65. In some embodiments the **heat shock protein** of the method is human HSP60. In some embodiments the **heat shock protein** is chlamydial HSP60. The compns. is of particular value in the treatment of atherosclerosis.

L201 ANSWER 50 OF 56 TOXCENTER COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:218218 TOXCENTER
COPYRIGHT: Copyright 2004 ACS
DOCUMENT NUMBER: CA13401002328X
TITLE: Human **heat shock protein** 60 in diagnosis and treatment of atherosclerosis and coronary heart disease
AUTHOR(S): Singh, Mahavir; Prohaszka, Zoltan; Fust, Gyorgy; Romics, Laszlo
CORPORATE SOURCE: ASSIGNEE: Semmelweis University of Medicine
PATENT INFORMATION: WO 2000072023 A2 30 Nov 2000
SOURCE: (2000) PCT Int. Appl., 47 pp.
CODEN: PIXXD2.
COUNTRY: HUNGARY
DOCUMENT TYPE: Patent
FILE SEGMENT: CAPLUS
OTHER SOURCE: CAPLUS 2000:842379
LANGUAGE: English
ENTRY DATE: Entered STN: 20011116
Last Updated on STN: 20020305

AB The present invention concerns novel uses for human **HSP60** (**heat shock protein** 60) in methods of treatment or diagnosis of the human body, more particularly diagnostic test methods, the manufacture of diagnostic tests, and diagnostic test kits for patients with **vascular disorders** due to atherosclerosis, having a tendency to **heat shock protein**-induced

complement activation, for example to myocardial **disorders** such as coronary heart **disease**. Blood samples were applied to microtiter plates coated with recombinant hHSP60 and anti-hHSP60 antibodies were allowed to bind. Unbound material was washed away and peroxidase conjugated anti-complement C4b was added to detect complement activation. There was a pos. correlation between the level of anti-hHSP60 antibodies and coronary heart disease due to atherosclerosis. Children at risk due to family history had significantly elevated levels as well.

L201 ANSWER 51 OF 56 TOXCENTER COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:23991 TOXCENTER
DOCUMENT NUMBER: PubMed ID: 9498159
TITLE: Effect of combined heat, ozonation and ultraviolet irradiation (VasoCare) on **heat shock protein** expression by peripheral blood leukocyte populations
AUTHOR(S): Bulmer J; Bolton A E; Pockley A G
CORPORATE SOURCE: Clinical Sciences Centre, University of Sheffield, UK
SOURCE: Journal of biological regulators and homeostatic agents, (1997 Jul-Sep) 11 (3) 104-10.
Journal Code: 8809253. ISSN: 0393-974X.
COUNTRY: Italy
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
FILE SEGMENT: MEDLINE
OTHER SOURCE: MEDLINE 1998159594
LANGUAGE: English
ENTRY DATE: Entered STN: 20011116
Last Updated on STN: 20011116

AB The re-administration of whole blood subjected to heat, ozonation and ultraviolet irradiation (VasoCare therapy) has been shown to elicit clinical benefits in individuals with vascular disease. Given that these stressors induce **heat shock protein** (Hsp) expression and that **heat shock protein** reactivity is implicated in the pathogenesis of **vascular disease**, this study assessed the effect of VasoCare on intracellular expression of **Hsp60** and Hsp70 by treated peripheral blood leukocytes. Contrary to expectations, VasoCare induced a significant reduction (approximately 40%) in the proportion of peripheral blood mononuclear cells expressing intracellular Hsp60 and Hsp70, whereas it had no effect on **heat shock protein** expression by peripheral blood neutrophils. Cell surface **heat shock protein** expression was not detectable. The reduced expression of Hsp60 by mononuclear cells was concomitant with an increase in the levels of Hsp60 in treated plasma. Although the mechanism underlying the clinical effectiveness of VasoCare therapy has yet to be established, it may be that re-administration of treated blood or soluble factors derived therefrom modifies in vivo immune responsiveness to **heat shock proteins** or associated molecules.

L201 ANSWER 52 OF 56 USPATFULL on STN
ACCESSION NUMBER: 2003:232060 USPATFULL
TITLE: Vaccine adjuvant
INVENTOR(S): Minion, F. Chris, Ames, IA, UNITED STATES
Menon, Sreekumar A., Philadelphia, PA, UNITED STATES
Mahairas, Gregory G., Seattle, WA, UNITED STATES
PATENT ASSIGNEE(S): Iowa State University Research Foundation, Inc., an Iowa corporation (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003162260	A1	20030828
APPLICATION INFO.:	US 2003-384948	A1	20030310 (10)

RELATED APPLN. INFO.: Division of Ser. No. US 2000-692064, filed on 19 Oct 2000, GRANTED, Pat. No. US 6537552

	NUMBER	DATE

	NUMBER	DATE
PRIORITY INFORMATION:	US 1999-160249P	19991019 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: FISH & RICHARDSON P.C., 3300 DAIN RAUSCHER PLAZA, 60 SOUTH SIXTH STREET, MINNEAPOLIS, MN, 55402
NUMBER OF CLAIMS: 7
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 7 Drawing Page(s)
LINE COUNT: 1632
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention features fusion agents such as fusion proteins that are useful for the treatment of and prevention from diseases that are susceptible to the effects of cellular (Th1 type) immune responses. Also encompassed by the invention are nucleic acids encoding the fusion proteins of the invention, vectors containing the nucleic acids, and cells containing the vectors. The invention includes methods of making and using the fusion agents of the invention.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L201 ANSWER 53 OF 56 USPATFULL on STN
ACCESSION NUMBER: 2003:81455 USPATFULL
TITLE: Vaccine adjuvant
INVENTOR(S): Minion, F. Chris, Ames, IA, United States
Menon, Sreekumar A., Philadelphia, PA, United States
Mahairas, Gregory G., Seattle, WA, United States
PATENT ASSIGNEE(S): Iowa State University Research Foundation, Ames, IA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6537552	B1	20030325
APPLICATION INFO.:	US 2000-692064		20001019 (9)

	NUMBER	DATE
PRIORITY INFORMATION:	US 1999-160429P	19991019 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Smith, Lynette R. F.
ASSISTANT EXAMINER: Shahnan-Shah, Khatol S
LEGAL REPRESENTATIVE: Fish & Richardson P.C.
NUMBER OF CLAIMS: 8
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 10 Drawing Figure(s); 7 Drawing Page(s)
LINE COUNT: 1611
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention features fusion agents such as fusion proteins that are useful for the treatment of and prevention from diseases that are susceptible to the effects of cellular (Th1 type) immune responses. Also encompassed by the invention are nucleic acids encoding the fusion proteins of the invention, vectors containing the nucleic acids, and cells containing the vectors. The invention includes methods of making and using the fusion agents of the invention.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L201 ANSWER 54 OF 56 USPATFULL on STN
ACCESSION NUMBER: 2001:229399 USPATFULL
TITLE: Antigen-specific immune complex-based enzyme-linked immunosorbent assay
INVENTOR(S): Racis, Stanley Paul, North Sioux City, SD, United States

	NUMBER	KIND	DATE

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2001051351	A1	20011213
APPLICATION INFO.:	US 2001-816271	A1	20010323 (9)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2000-192472P	20000327 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: KIRKPATRICK & LOCKHART LLP, 535 SMITHFIELD STREET, PITTSBURGH, PA, 15222
NUMBER OF CLAIMS: 71
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 4 Drawing Page(s)
LINE COUNT: 1718
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention is in the field of immunologic serological in vitro diagnostics. The invention is an ELISA-based diagnostic testing system and method that provides the capability to "look within" and measure an immune complexes specific antigen and antibody using typical ELISA microplates and procedures. One aspect of the invention is a method for detecting antigen and antibody in immune complexes. A second aspect of the invention is for a well design that may be used in the method of the invention. A third aspect of the invention is for a kit for detecting antigen, antibody, or both antigen and antibody in immune complexes.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L201 ANSWER 55 OF 56 USPATFULL on STN
ACCESSION NUMBER: 2001:229235 USPATFULL
TITLE: METHOD FOR USING SOLUBLE CURCUMIN TO INHIBIT PHOSPHORYLASE KINASE IN INFLAMMATORY DISEASES
INVENTOR(S): HENG, MADALENE C.Y., NORTHRIDGE, CA, United States

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2001051184	A1	20011213
APPLICATION INFO.:	US 1999-315856	A1	19990520 (9)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: ATTN: DAVID A. FARAH. M.D., SHELDON & MAK, 225 SOUTH LAKE AVENUE, SUITE 900, PASADENA, CA, 91101
NUMBER OF CLAIMS: 115
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 13 Drawing Page(s)
LINE COUNT: 4191
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The compound curcumin, derived from turmeric, inhibits phosphorylase kinase and, by doing so, exhibits a number of physiological effects related to the control of inflammation and cellular proliferation. However, curcumin is effective only when in solution. Curcumin is almost completely insoluble in water or in oils, but is soluble in alcohols. Accordingly, a method for treating inflammation in a mammal comprising administering curcumin in a solution containing at least one alcohol to a mammal to detectably inhibit the activity of phosphorylase kinase in the blood of the mammal or in a tissue of the mammal. The alcohol is preferably ethanol, 1-propanol, or 2-propanol; most preferably, it is ethanol. Instead of curcumin, a curcumin derivative or curcuminoid can be administered. The method can further comprise the administration of at least one additional compound that can be (1) vitamin D.sub.3 and vitamin D.sub.3 analogues; (2) vitamin A, vitamin A derivatives, and vitamin A analogues (3) a calmodulin inhibitor; (4) an anti-inflammatory drug; (5) a calcium channel blocker; (6) a H1 or H2 histamine blocker; (7) an antioxidant; (8) a polyphenolic compound; (9) a monoterpene; (10) genistein; (11) a soybean derived lectin; and (12) dehydrozingerone. Another aspect of the present invention is a pharmaceutical composition

comprising curcumin, a curcuminoid, or a curcumin derivative in a solution containing at least one alcohol, at least one additional compound as described above, and a pharmaceutically acceptable carrier.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L201 ANSWER 56 OF 56 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2003-239361 [23] WPIDS
DOC. NO. CPI: C2003-061460
TITLE: Assessing injury e.g. stroke, diabetes, hypoxia injury in subject, by determining pattern of expression exhibited by blood cells obtained from subject and comparing the expression to an injury database.
DERWENT CLASS: B04 D16
INVENTOR(S): LU, A; SHARP, F R; TANG, Y
PATENT ASSIGNEE(S): (LUAA-I) LU A; (SHAR-I) SHARP F R; (TANG-I) TANG Y; (UYCI-N) UNIV CINCINNATI
COUNTRY COUNT: 96
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2003008647	A2	20030130	(200323)*	EN	126

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

US 2003104393	A1	20030605 (200339)	

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2003008647	A2	WO 2001-US44278	20011128
US 2003104393	A1 Provisional	US 2000-253568P	20001128
		US 2001-996275	20011128

PRIORITY APPLN. INFO: US 2000-253568P 20001128; US 2001-996275 20011128
AN 2003-239361 [23] WPIDS
AB WO2003008647 A UPAB: 20030407
NOVELTY - Assessing (M) injury in an individual comprising determining a pattern of expression exhibited by blood cells obtained from the individual, and comparing the pattern of expression exhibited by the obtained blood cells to an injury database to assess the injury, is new.
USE - (M) is useful for assessing injury caused as a result of cell death, cell dysfunction, genetic abnormalities, in an individual. (M) is useful for stroke injury including ischemic and/or hemorrhagic stroke injury assessment, hypoxia injury, hypoglycemia injury assessment, movement disorder injury assessment, genetic disorder injury (neurofibromatosis) assessment using a single blood sample, psychosis (e.g. bipolar, schizophrenia), headache (acute migraine headache), organ, brain, stroke, seizure, hypoglycemia, hypoxia, diabetes, infectious disease (tuberculosis, viral and/or prion), immune mediated disease assessment, efficacy or toxicity or proliferative disease assessment (neurofibromatosis). The seizure injury comprises status epilepticus, single tonic-clonic seizure, syncope or pseudo-seizure. The movement disorder injury includes Parkinson's, Huntington's disease, Tourette's, Sydenhams Chorea, Diffuse Lewy body disease, or corticobasal ganglionic disease. The immune mediated disease include Graves, rheumatoid arthritis, thyroiditis/hypothyroidism, vitiligo, insulin-dependent diabetes mellitus (IDDM), multiple sclerosis, primary glomerulonephritis, systemic lupus erythematosus, Sjogren's, asthma and transplant rejection. (All claimed.)

ADVANTAGE - The method can be used to assess injury that cannot be conveniently or adequately evaluated by current blood tests, by imaging or biopsy, and may conveniently be used on all individuals, including individuals who are asymptomatic, in altered states of consciousness, and/or who are artificially ventilated. The methods are relatively non-invasive and do not require biopsy or the injection of radioisotopes or radiopaque dyes.
Dwg.0/10

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